Association of Hospital-level Neuraxial Anesthesia Use for Hip Fracture Surgery with Outcomes

A Population-based Cohort Study

Daniel I. McIsaac, M.D., M.P.H., F.R.C.P.C., Duminda N. Wijeysundera, M.D., Ph.D., F.R.C.P.C., Allen Huang, M.D., F.R.C.P.C., Gregory L. Bryson, M.D., F.R.C.P.C., M.Sc., Carl van Walraven, M.D., F.R.C.P.C., M.Sc.

ABSTRACT

Background: There is consistent and significant variation in neuraxial anesthesia use for hip fracture surgery across jurisdictions. We measured the association of hospital-level utilization of neuraxial anesthesia, independent of patient-level use, with 30-day survival (primary outcome) and length of stay and costs (secondary outcomes).

Methods: We conducted a population-based cohort study using linked administrative data in Ontario, Canada. We identified all hip fracture patients more than 65 yr of age from 2002 to 2014. For each patient, we measured the proportion of hip fracture patients at their hospital who received neuraxial anesthesia in the year before their surgery. Multilevel, multivariable regression was used to measure the association of log-transformed hospital-level neuraxial anesthetic-use proportion with outcomes, controlling for patient-level anesthesia type and confounders.

Results: Of 107,317 patients, 57,080 (53.2%) had a neuraxial anesthetic; utilization varied from 0 to 100% between hospitals. In total, 9,122 (8.5%) of patients died within 30 days of surgery. Survival independently improved as hospital-level neuraxial use increased ($P = 0.009$). Primary and sensitivity analyses demonstrated that most of the survival benefit was realized with increase in hospital-level neuraxial use above 20 to 25%; there did not appear to be a substantial increase in survival above this point. No significant associations between hospital neuraxial anesthesia-use and other outcomes existed.

Conclusions: Hip fracture surgery patients at hospitals that use more than 20 to 25% neuraxial anesthesia have improved survival independent of patient-level anesthesia type and other confounders. The underlying causal mechanism for this association requires a prospective study to guide improvements in perioperative care and outcomes of hip fracture patients.

Visual Abstract: An online visual overview is available for this article at http://links.lww.com/ALN/B634. (**ANESTHESIOLOGY** 2018; 128:480-91)

MORTALITY and adverse events are common after hip fracture surgery. Major postoperative complications occur in more than 20% of patients,[1] and more than one third of hip fracture patients die within 6 months of their injury.[2] Therefore, strategies to improve postoperative outcomes for hip fracture patients are needed.

The choice of general anesthesia (GA) *versus* neuraxial anesthesia (NA) is postulated to impact outcomes after hip fracture surgery. Possible mechanisms whereby NA might improve outcomes include avoidance of respiratory complications, mitigation of the surgical stress response, reduced exposure to blood product transfusion, and enhanced functional recovery.[3] However, contemporary studies comparing GA *versus* NA with respect to outcomes after hip fracture surgery provide conflicting

> **What We Already Know about This Topic**
>
> - Wide hospital-level variation exists in the use of neuraxial anesthesia for hip fracture surgery
> - There are conflicting real-world data regarding the association of anesthesia type with decreased mortality
>
> **What This Article Tells Us That Is New**
>
> - Across hospitals in Ontario, Canada, the rate of neuraxial anesthesia use for hip fracture surgery varied from 0 to 100%
> - Hospitals performing neuraxial anesthesia for more than 20 to 25% of their patients demonstrated improved survival compared to hospitals performing below that threshold

conclusions.[1,3–7] Despite this uncertainty, several practice guidelines already recommend the use of NA over GA.[8–11]

<zdoi;10.1097/ALN.0000000000001899>

The uncertainty about which anesthetic technique is superior for hip fracture surgery is reflected in real-world practice. Large observational studies have found substantial interinstitutional practice variation in the use of NA for hip fracture surgery. Recent data from the United Kingdom found an eightfold variation in use of NA for hip fracture surgery between different hospitals[12]; data from the United States also suggest substantial between-hospital variation.[5] In elective surgery, variation in perioperative care has been associated with adverse outcomes after major noncardiac surgery.[13] Although some variation in practice is warranted due to baseline differences between patients that may contraindicate one anesthetic technique *versus* another, differences in patient-level characteristics are unlikely to account for the degree of variation that has been documented.[14]

Understanding the impact of variation in anesthesia care on outcomes after hip fracture surgery is needed to inform clinical care and health policy.[15] In this study, we hypothesized that patients who had their hip fracture surgery in hospitals that utilized a higher proportion of NA would have improved postoperative survival, shorter length of hospital stay, and lower overall costs of care in the 30 days after surgery.

Materials and Methods

Setting and Data

After ethics approval from the Sunnybrook Health Sciences Center Research Ethics Board (Toronto, Canada), we conducted a population-based cohort study in Ontario, Canada, where hospital and physician services are provided to all residents through a publicly funded healthcare system and are recorded in health administrative data sets that are collected using standardized methods.[16,17] All data were linked deterministically using encrypted patient-specific identifiers at the Institute for Clinical Evaluative Sciences (ICES), an independent research institute that houses the health administrative data for the province of Ontario. The data sets used for the study included the Discharge Abstract Database (DAD), which captures all hospitalizations; the Ontario Health Insurance Plan (OHIP) database, which captures physician service claims; the National Ambulatory Care Reporting System, which captures details of all emergency and outpatient care; the Continuing Care Reporting System, which records details of long-term and respite care; the Ontario Drug Benefits Database, which captures prescription drug claims for residents 65 yr and older; the ICES Physician Database, which contains information on physician specialty, demographics, training, and practice patterns and which draws these data from the OHIP Corporate Provider Database, the Ontario Physician Human Resource Data Center database, and the OHIP database of physician billings; and the Registered Persons Database (RPDB), which captures all death dates for residents of Ontario. The analytic data set was created by a trained data analyst independent from the study team. Because the analytic data was generated from data normally collected at ICES, no further data

processing was required. Analysis was performed by the lead author and overseen by the senior author. The study protocol was registered (clinicaltrials.gov NCT02787031), and this manuscript is reported per the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) and the REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) guidelines.[18,19]

Cohort

We identified all Ontario residents who were 66 yr or older on the day of their emergency hip fracture surgery and who were cared for in a hospital that had performed at least 10 emergency hip fracture surgeries in the previous year. These patients were identified using Canadian Classification of Interventions codes to identify hip fracture surgery (diagnostic code S72 for hip fracture and then procedural codes 1VA53, 1VA74, 1VC74, or 1SQ53).[20] Reabstraction studies demonstrate a high level of agreement between abstractors when identifying hip fracture patients having surgery with these codes (κ, 0.95; positive predictive value, 0.95 [95% CI, 0.94 to 0.97]).[21] Furthermore, we limited our sample to individuals who were admitted to hospitals on an urgent basis to exclude elective hip replacement operations. Participants were identified from April 2002 (the date of introduction of the *International Classification of Diseases*, Tenth Edition, to identify diagnoses and the Canadian Classification of Interventions to identify procedures) to March 2014 (the latest time at which all data sets were complete). This was a patient-level analysis and included only the first hip fracture surgery during the study period for any individual. Patients were excluded if their anesthesia type was missing from their administrative record.

Exposure

Anesthesia type was captured from the DAD, where an anesthesia type is coded for every operative procedure; reabstraction demonstrated 94% agreement for this field.[22] Anesthesia type was coded in the DAD as general, spinal, epidural, or combined general and neuraxial (epidural or spinal). Patients who received an epidural or spinal anesthetic without concurrent GA were categorized as having received NA, whereas any patient who received a GA (including those who had a combined GA and NA) were categorized as not having received NA.

Our exposure of interest was the proportion of patients at a given hospital who had NA for emergency hip fracture surgery in the year before each patient's surgery. Although we performed a patient-level analysis, all hip fracture cases at each hospital were included in calculating the proportion of NA use. For each patient this was calculated as: the number of emergency hip fracture surgery patients at the index hospital in the year before a patient's surgery who had NA (this was the numerator) divided by the total number of emergency hip fracture surgeries at that patient's hospital in the year before that patient's surgery (this was the denominator). By determining the proportion based on the year before each patient's surgery, we were able to account for changes in

hospital structure and process over the course of our study period.[23]

To remove assumptions of linearity and to account for the distribution of the proportion, which was heavy-tailed,[24] our prespecified approach was to transform the hospital-level proportion of NA use for emergency hip fracture surgery using the natural logarithm. Compared to categorization, this approach also avoids information loss.[25] As sensitivity analyses, we determined the best continuous fit using fractional polynomials[26] (a linear fit was identified as the best fit), and we also categorized the proportion of NA use by dividing hospitals into quintiles of NA use with the lowest quintile as the reference category.

Outcomes

The primary outcome was survival in the 30 days after surgery. All deaths were captured from the RPDB, which includes all deaths from any cause in any jurisdiction for all residents of Ontario. There were two secondary outcomes: postoperative length of stay (LOS), which was calculated as the date of hospital discharge minus the date of surgery from the DAD (patients who remained in hospital beyond 365 days after surgery were censored); and total costs of care incurred by the provincially funded universal healthcare system in the 30 days after surgery (this includes the day of surgery), which were calculated using standardized patient-level costing algorithms (costs are expressed in 2014 Canadian dollars).[27]

Covariates

Patient demographics were identified from the RPDB and from the Canadian Census. Standard methods were used to identify all Elixhauser comorbidities based on International Classification of Diseases (ICD)-9 and ICD-10 codes from the DAD in the 3 yr preceding surgery.[28] We also measured the preoperative LOS. We identified from Ontario Drug Benefits Database receipt of the following prescription medications in the 6 months before surgery (because we felt that these agents or the conditions for which they were indicated could confound the anesthesia type-outcome association): angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, antiarrhythmics, anticoagulants, antidepressants, antipsychotics, antiplatelet agents, benzodiazepines, β-blockers, dementia drugs (donepezil, rivastigmine, memantine, or galantamine), digoxin, inhaled bronchodilators, inhaled corticosteroids, insulin, oral corticosteroids, and oral antihyperglycemics. We identified use of an intraoperative arterial line from the OHIP database. Expected patient longevity was gauged using the Hospital-patient One-year Mortality Risk score, an externally validated model for 1-yr all-cause mortality with excellent discrimination (c-statistic, 0.89 to 0.92) and calibration.[29]

We also identified information about each patient's anesthesiologist and hospital. We determined each physician's age, sex, years of experience (calculated as year of surgery – [year of anesthetist graduation + 5 yr for residency training]), and their full-time equivalency status based on their annual billings compared to that year's average from all physicians in the specialty. We determined each hospital's teaching status and its volume of hip fracture surgeries in the year before each study patient's hip fracture surgery.

Analysis

SAS version 9.4 (SAS Institute, USA) was used for all analyses. Descriptive statistics were used to compare patient, anesthesiologist, and hospital characteristics across NA utilization quintiles. As recommended, all adjusted models accounted for clustering of patients within hospitals, which were the highest level of hierarchy in our data.[30] Proportional hazards models accounted for clustering using a robust sandwich covariance matrix estimate; we included a random intercept term for each hospital in our generalized linear models.

All exposure-outcome associations were measured on an unadjusted basis and after multilevel multivariable adjustment. In addition to the exposure, all adjusted models included covariates that we postulated could confound the exposure–outcome relationship. These covariates included patient-level variables (the type of anesthesia that each patient received [isolated NA vs. GA of any type], patient age [represented as 66 to 74 or 75 and older as recommended by the National Surgical Quality Improvement Program universal risk calculator[31]], sex [male or female], Hospital-patient One-year Mortality Risk score [as a continuous linear variable, its recommended form[32]], rural residence [binary], neighborhood income quintile [five-level categorical variable], all Elixhauser comorbidities [as binary variables], preoperative LOS [categorical: 0 to 1 days, 2 days, or greater than 2 days], whether surgery was performed on a weekend [binary], any acute care hospitalization in the year before the index hospital admission [binary], any emergency department visit in the year before the index hospital admission [binary], use of an intraoperative arterial line [binary], each prescription medication described above under "Covariates" [as binary variables], and year of surgery [restricted cubic spline with three knots]), provider-level variables (anesthesiologist sex [binary], anesthesiologist age quintile [five-level categorical variable], anesthesiologist years in practice quintile [five-level categorical variable], and anesthesiologist's full-time equivalency quintile [five-level categorical variable]), and hospital-level variables (teaching status [binary] and annual volume of emergency hip fracture surgeries quintile [five-level categorical variable]).

For our primary analysis of 30-day survival, we used proportional hazards regression to model time to death. Adherence to the proportional hazards assumption was verified using log-negative log plots. Because our exposure was transformed using the natural logarithm, the regression coefficient was not directly interpretable as a hazard ratio. Therefore, we calculated the specific adjusted hazard ratio (HR) for each value from 1% NA use to 100% NA use and created a figure to display the HR and 95% CI for each value in this range.

Secondary outcome analyses included the same covariates as the primary outcome analysis. For LOS, we also used proportional hazards regression to model time to hospital discharge (in this analysis regression coefficients more than 0 indicate a shorter LOS); however, in-hospital mortality was a competing risk for this outcome. Therefore, we used the methods of Fine and Gray[33] to calculate the subdistributional hazard function. Adherence to the proportional hazards assumption was verified using log-negative log plots. For costs (which had skewed distributions), a generalized multilevel linear model with γ distributed errors and a logarithmic link was employed.[34]

Sensitivity Analyses

We performed prespecified and *post hoc* sensitivity analyses; all analyses were adjusted for the same covariates as our primary adjusted analysis. First, we performed a fractional polynomial analysis that recommended a linear form as the best-fitting continuous representation for the association of hospital-level NA use with survival. Therefore, we replaced the log-transformed variable in the primary adjusted analysis with a continuous linear measure or hospital-level NA use and measured its association with 30-day survival. Next, we created an ordinal representation of hospital-level NA use, with cutoffs established using the RANK procedure in SAS, to create five equal groups representing quintiles of hospital-level NA use. We then entered the quintile variable into our primary adjusted regression model (with the lowest quintile of NA use as the reference category) and measured its association with 30-day survival. For our last prespecified sensitivity analysis, we repeated the primary adjusted analysis in a restricted cohort of participants who had only an isolated spinal or an isolated GA (*i.e.*, epidural and combined NA with GA patients were excluded).

Our *post hoc* analysis involved measuring the association of the log-transformed proportion of hospital-level NA use, restricting the analysis first only to people who had NA and then only to people who had a GA to further isolate the impact of hospital-level NA use from the impact of patient-level anesthesia type. Finally, during the peer review process, it was suggested that hospitals whose surgical times were longer might be less likely to use NA and that longer surgical time might also lead to decreased survival. Therefore, using previously described methods,[35] we estimated the average surgical time at each hospital from physician billing data and added this to the model used in our primary analysis as a five-level categorical variable representing quintiles of average surgical time.

Process Analyses

After completion of our prespecified analyses, we calculated the proportion of patients in each quintile of NA-use hospitals who received certain interventions or processes of care that were measurable in our data and that could contribute to the difference in mortality between NA use quintiles. The interventions and processes included receipt of a preoperative anesthesiology consultation, pre- or postoperative geriatric medicine consultation, pre- or postoperative general medicine consultation, a wait from admission to operating room of 2 days or less (which is the wait time standard in Ontario[20]), and receipt of a peripheral nerve block.

Missing Data

Outcome data was complete for all participants. Anesthesia type was missing for 96 people (0.08%); these cases were excluded from all analyses. Rural residency status was missing for 0.09% and was imputed with the most common value (not rural). Income quintile was missing and imputed with the group median (quintile 3) for 0.5% of participants.

Results

We identified 107,317 hip fracture surgery patients from 80 different hospitals aged more than 65 yr who had a valid anesthesia type entered in their DAD record. NA without concurrent GA was used in 57,080 (53.2%) patients. Overall NA use increased from 40% in 2002 to 53% in 2013 and 2014 (fig. 1). Of the patients receiving GA, 3.1% had a concurrent NA. A spinal anesthetic was placed in 98.9% of patients having NA without GA. The proportion of hip fracture surgeries in each hospital that used NA varied extensively (median = 53%; range = 0 to 100%). In the lowest NA-utilization quintile, NA use ranged from 0 to 27.4%; in the second lowest quintile, it ranged from 27.5 to 46.0%; in quintile 3, it ranged from 46.1 to 59.1%; in quintile 4, it ranged from 59.2 to 71.1%; and in the highest NA-use quintile, it ranged from 71.2 to 100%. Characteristics by quintile of NA utilization proportion are provided in table 1.

Death within 30 days of surgery occurred in 9,122 (8.5%) individuals. Median hospital LOS was 9 days (interquartile range = 6 to 18); 6,976 (6.5%) patients died in the hospital before being discharged. The median cost per patient to the universal health insurance program in the 30 days after and
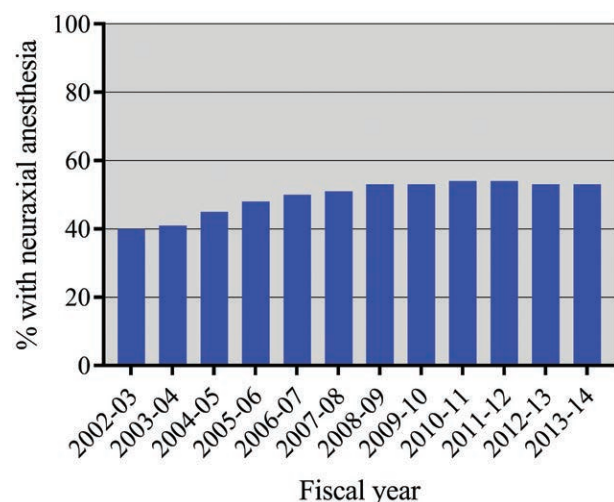
Fig. 1. The proportion of hip fracture surgery patients receiving neuraxial anesthesia without concurrent general anesthesia by fiscal year over the study period.

Table 1. Patient Characteristics by Quintile of Hospital-level Neuraxial Anesthesia Utilization

	Lowest NA Utilization Quintile	Quintile 2	Quintile 3	Quintile 4	Highest NA Utilization Quintile	P Value
Range of NA utilization (%)	0–27.4	27.5–46.0	46.1–59.1	59.2–71.1	71.1–100	
n	22,332	22,655	21,700	21,313	19,317	
Demographics						
Age, mean, (SD)	83 (8)	83 (8)	83 (8)	83 (7)	83 (8)	< 0.0001
Female, %	73.6	73	72.9	73.9	73.7	0.06
Rural, %	11.3	10.2	13.4	12.8	17.8	< 0.0001
Neighborhood income quintile, median (IQR)	3 (4, 5)	3 (4, 5)	3 (4, 5)	3 (4, 5)	3 (4, 5)	< 0.0001
Comorbidities						
Alcohol abuse, %	2	2.1	2.1	2.3	2.1	0.27
ASA score < 3	18.1	13.4	11.9	15.1	13	< 0.0001
Atrial arrhythmia, %	9.3	9.4	9.6	9.1	8.9	0.12
Blood loss anemia	17.9	16.8	17.2	20.5	16.1	< 0.0001
Cardiac valvular disease, %	3.6	3.7	3.8	3.6	3.1	< 0.0001
Cerebrovascular disease, %	6.3	6.4	6	6.3	6.5	0.18
Chronic obstructive pulmonary disease, %	11.8	12.2	12.9	12.8	13.7	< 0.0001
Coagulopathy, %	4	3.3	3.1	3	2.7	< 0.0001
Deficiency anemia	1.4	0.9	0.9	1	1.1	< 0.0001
Dementia, %	8.8	9	10.2	10.1	10.6	< 0.0001
Depression, %	4.9	4.7	4.7	4.5	4.8	0.36
Diabetes mellitus without complications, %	12.4	13.1	12.1	12.2	12.1	0.007
Diabetes mellitus with complications, %	7.4	9.6	10.8	10.7	10.9	< 0.0001
Dialysis, %	1.2	1.1	1.5	1.7	0.8	< 0.0001
Disease of pulmonary circulation, %	2.3	2.3	2.3	2.3	2	0.04
Drug abuse, %	0.5	0.3	0.5	0.3	0.4	0.006
Heart failure, %	14.3	13.5	13.3	14	13.2	0.009
Hemiplegia, %	1.2	1.1	0.9	1.1	1.1	0.016
Hypertension without complications, %	36	39.9	36.8	37.2	34.9	< 0.0001
Hypertension with complications, %	2.8	2.6	2.9	2.6	2.4	0.031
Liver disease, %	0.8	0.7	0.7	0.7	0.7	0.31
Malignancy, %	5.8	5.4	5.3	5.3	5.3	0.07
Metastases, %	1.7	1.5	1.6	1.7	1.6	0.43
Obesity, %	0.8	1	1	1	0.9	0.15
Peptic ulcer disease, %	1.5	1.3	1.1	1.3	1.1	0.001
Peripheral vascular disease, %	2.5	2.4	2.5	2.5	2.5	0.9
Psychoses, %	1.9	1.3	1.3	1.4	1.3	< 0.0001
Renal disease, %	4.1	4.4	4.6	4.5	4.3	0.04
Rheumatic disease, %	1.4	1.2	1.3	1.2	1.2	0.26
Venous thromboembolism, %	1.1	1	0.9	0.9	0.8	0.0004
1-yr mortality risk, mean (SD)	38 (5)	39 (5)	39 (5)	39 (5)	39 (5)	< 0.0001
Healthcare resource use						
Hospitalization in last year, %	26.3	27.5	26.8	26.7	26.2	0.08
Emergency department visit in last year, %	59.4	60.7	62.3	61.5	60.2	< 0.0001
Type of hip fixation						< 0.0001
Implantation of internal device						
Pelvis, %	1.1	0.6	0.5	0.5	0.2	
Hip joint, %	39.5	38.9	38.9	39.2	39.4	
Fixation						
Hip joint, %	25	24.2	25	24.4	22.4	
Femur, %	34.5	36.4	35.7	35.9	38	
Anesthesia care						
Arterial line, %	15.4	10.8	8.5	8.9	6.3	< 0.0001
Neuraxial anesthesia, %	20.7	41.1	58.6	69.6	81.9	< 0.0001

(*Continued*)

Table 1. (Continued)

	Lowest NA Utilization Quintile	Quintile 2	Quintile 3	Quintile 4	Highest NA Utilization Quintile	P Value
Prescription drugs						
ACE-I/ARB, %	40	42.6	43	43	42.9	< 0.0001
Antiarrhythmic, %	3.6	3.4	3.4	2.6	2.8	< 0.0001
Anticoagulant, %	12.3	13	14.3	13.5	12.9	< 0.0001
Antidepressant, %	30.1	31.5	33.8	33.4	35.1	< 0.0001
Antiplatelet agent, %	5.5	7	7.8	7.4	7.8	< 0.0001
Antipsychotic, %	12.8	13.1	14.3	14.2	15.0	< 0.0001
Benzodiazepine, %	27.1	25.4	25.6	25.6	26.2	< 0.0001
β-Blocker, %	27.2	27.7	28	27.8	27.4	< 0.0001
Dementia drug, %	10.9	12.3	13.9	13.3	13.6	< 0.0001
Digoxin, %	6.6	5.8	5.7	6.1	5.5	< 0.0001
Inhaled bronchodilator, %	12.9	13.6	14.9	14.9	15.5	< 0.0001
Inhaled corticosteroid, %	10.2	11.1	12.2	12.3	12.9	< 0.0001
Insulin, %	4.1	4.2	4.5	4.7	4.6	0.004
Oral corticosteroid, %	6.5	6.8	7.1	7.3	6.8	0.004
Oral diabetes agent, %	11.2	12.6	12.4	12.5	12.6	< 0.0001
Anesthesiologist characteristics						
Full-time equivalency, mean (SD)	1.1 (0.2)	1.1 (0.2)	1.1 (0.2)	1.1 (0.2)	1.1 (0.3)	< 0.0001
Age, mean (SD)	48 (10)	48 (10)	47 (9)	47 (9)	47 (9)	< 0.0001
Years in practice, mean (SD)	17 (10)	17 (10)	16 (10)	16 (10)	16 (10)	< 0.0001
Female anesthesiologist, %	22.6	23.5	23.6	25.1	19.2	< 0.0001
Hospital characteristics						
Yearly no. of hip fracture surgeries, mean (SD)	256 (181)	203 (72)	223 (84)	216 (90)	194 (84)	< 0.0001
Teaching hospital, %	55.6	22.8	25.6	31.9	12.9	< 0.0001
Preoperative LOS > 2 days, %	10.4	7.3	7	7.4	7.2	< 0.0001

ACE-I/ARB = angiotensin converting enzyme inhibitor/angiotensin receptor blocker; ASA = American Society of Anesthesiologists; IQR = interquartile range; LOS = length of stay; NA = neuraxial anesthesia.

including hip fracture surgery was \$22,138 (interquartile range, \$16,430 to \$28,354).

The crude association between the log-transformed proportion of hospital-level NA use and 30-day survival was not significant ($P = 0.7$, regression coefficient = 0.015). After multilevel multivariable adjustment, the association of log-transformed hospital-level NA use with 30-day survival was significant ($P = 0.009$; regression coefficient = −0.091). Model diagnostics demonstrated good discrimination, with a c-statistic of 0.84. The full parameters for our adjusted survival model are provided in table 2. Figure 2 illustrates the change in survival as the proportion of hospital-level NA use increased. As the proportion increased above 5%, the adjusted HR decreased below 1 (the null value), whereas at approximately 20% hospital-level NA use, there was an inflection point where the slope of the line describing association between proportion of NA-use and survival flattened. Despite this, however, there continued to be improved survival as the NA-use proportion increased toward 100% (adjusted HR at 100% NA use = 0.87; 95% CI, 0.78 to 0.97).

Length of stay and 30-day total health system costs were not significantly associated with the log-transformed proportion of NA use on a crude basis ($P = 0.18$, regression coefficient = 0.0057 for LOS; $P = 0.055$, regression coefficient = −0.0034 for costs) or after multilevel multivariable adjustment ($P = 0.7$, regression coefficient = −0.01 for LOS; $P = 0.8$, regression coefficient = 0.0004 for costs).

Sensitivity Analyses

When the hospital-level NA-use proportion was expressed as a linear term, for every 10% increase in the proportion of NA utilization, 30-day survival increased by 3% (adjusted HR for 10% increase in NA use = 0.97; 95% CI, 0.96 to 0.98; $P < 0.001$). When hospital-level NA utilization was represented as a categorical variable based on quintiles of NA use, there was an overall increase in survival as the proportion of NA use increased (lowest NA-use quintile = reference; quintile 2 HR = 0.88, 95% CI, 0.80 to 0.97; quintile 3 HR = 0.90, 95% CI, 0.79 to 1.02; quintile 4 HR = 0.85, 95% CI, 0.76 to 0.95; highest NA-use quintile HR = 0.82, 95% CI, 0.72 to 0.94). When the highest quintile of hospital-level NA use was set as the reference category, only the lowest NA-use category had significantly reduced survival (highest NA-use quintile = reference; quintile 4 HR = 1.04, 95% CI, 0.97 to 1.11; quintile 3 HR = 1.09, 95% CI, 0.98 to 1.17; quintile 2 HR = 1.07, 95% CI, 0.99 to 1.15; lowest NA-use quintile HR = 1.22, 95% CI, 1.06 to 1.39). Restricting the analysis to patients who had only an isolated GA or a spinal anesthetic only, our results were similar to the primary analysis ($P = 0.01$, regression coefficient = −0.087).

Table 2. Model Specification for Adjusted Survival Model (Primary Analysis)

Variable	Regression Coefficient*		P Value
Natural logarithm of proportion of hospital-level NA utilization	−0.09134		0.009
Demographics	Hazard Ratio	95% CI	
Age ≥ 75	0.68	0.63–0.74	< 0.0001
Female	0.57	0.54–0.60	< 0.0001
Neighborhood income quintile lowest	Reference		
2	1.02	0.95–1.10	0.7
3	0.98	0.92–1.06	0.7
4	1.04	0.97–1.12	0.3
Highest	0.95	0.89–1.01	0.1
Rural	0.86	0.80–0.93	< 0.0001
Comorbidities			
ASA score 5	Reference		
4	0.23	0.19–0.28	< 0.0001
3	0.42	0.35–0.49	< 0.0001
≤ 2	0.15	0.12–0.19	< 0.0001
Alcohol abuse	0.87	0.75–1.01	0.07
Atrial arrhythmia	0.82	0.73–0.93	< 0.0001
Blood loss anemia	1.19	1.11–1.26	< 0.0001
Cardiac valvular disease	1.02	0.94–1.12	0.5
Cerebrovascular disease	0.99	0.90–1.10	0.8
Chronic obstructive pulmonary disease	1.10	1.02–1.18	0.01
Coagulopathy	1.21	1.08–1.35	0.002
Defficiency anemia	0.78	0.63–0.95	0.01
Dementia	1.08	1.02–1.15	0.02
Depression	0.78	0.70–0.88	< 0.0001
Diabetes mellitus without complications	0.88	0.81–0.96	0.03
Diabetes mellitus with complications	0.90	0.82–0.99	0.03
Dialysis	1.22	1.04–1.42	0.02
Disease of pulmonary circulation	1.53	1.32–1.77	< 0.0001
Drug abuse	0.68	0.45–1.04	0.08
Heart failure	1.80	1.70–1.91	< 0.0001
Hemiplegia	0.84	0.67–1.04	0.1
Hypertension without complications	0.85	0.81–0.90	< 0.0001
Hypertension with complications	1.13	1.02–1.26	0.02
Liver disease	1.30	1.10–1.54	0.002
Malignancy	1.01	0.94–1.08	0.8
Metastases	1.34	1.14–1.57	0.0004
Obesity	0.85	0.67–1.09	0.2
Peptic ulcer disease	0.84	0.70–1.01	0.06
Peripheral vascular disease	1.04	0.94–1.17	0.4
Psychoses	0.91	0.75–1.09	0.3
Renal disease	0.97	0.88–1.07	0.5
Rheumatic disease	0.76	0.61–0.95	0.008
Venous thromboembolism	0.85	0.68–1.07	0.2
Weight loss	1.17	1.06–1.30	0.001
HOMR score (for 1-point increase)	1.10	1.09–1.11	< 0.0001
Healthcare resource use			
Hospitalization in last year	1.00	0.95–1.05	0.9
Emergency department visit in last year	0.92	0.88–0.97	0.003

(Continued)

Table 2. (Continued)

Variable	Regression Coefficient*		P Value
Surgical characteristics			
Fixation, femur	Reference		
Implantation of internal device			
Pelvis	0.66	0.47–0.93	0.02
Hip joint	0.94	0.88–.01	0.3
Fixation, hip joint	0.97	0.92–1.03	0.1
Weekend surgery (*vs.* weekday)	1.02	0.98–1.06	0.4
Preoperative LOS 1 day	Reference		
2 days	0.83	0.78–0.89	< 0.0001
> 2 days	0.90	0.82–0.98	0.02
Year of surgery (restricted cubic spline)	0.95	0.93–0.97	< 0.0001
	1.00	0.98–1.02	0.9
Anesthesia care			
Arterial line	1.08	1.02 – 1.15	0.01
Neuraxial anesthesia (*vs.* general)	0.97	0.93–1.02	0.3
Prescription drugs			
ACE-I/ARB	1.05	1.01–1.10	0.02
Antiarrythmatic	0.82	0.73–0.93	0.002
Anticoagulant	1.09	1.01–1.18	0.03
Antidepressant	0.98	0.93–1.03	0.3
Antiplatelet agent	0.93	0.86–1.00	0.06
Antipsychotic	0.70	0.67–0.74	< 0.0001
Benzodiazepine	0.97	0.93–1.02	0.3
β-Blocker	0.97	0.93–1.02	0.2
Dementia drug	1.02	0.96–1.09	0.6
Digoxin	0.85	0.79–0.93	0.0002
Inhaled bronchodilator	0.96	0.90–1.04	0.3
Inhaled corticosteroid	1.04	0.94–1.14	0.4
Insulin	0.89	0.79–0.99	0.04
Oral corticosteroid	0.91	0.84–0.99	0.02
Oral diabetes agent	1.04	0.94–1.15	0.5
Anesthesiologist characteristics			
Full-time equivalency quintile highest	Reference		
4	1.18	1.10–1.28	0.008
3	1.12	1.04–1.20	0.04
2	1.08	1.00–1.18	0.001
Lowest	1.07	0.98–1.17	< 0.0001
Anesthesiologist age quintile highest	Reference		
4	0.96	0.80–1.16	0.06
3	1.00	0.84–1.19	0.7
2	1.04	0.88–1.22	0.9
Lowest	1.12	0.99–1.27	0.1
Anesthesiologist experience quintile highest	Reference		
4	1.08	0.90–1.29	0.2
3	1.08	0.91–1.29	0.7
2	1.03	0.87–1.21	0.4
Lowest	0.93	0.82–1.05	0.4
Female anesthesiologist (*vs.* male)	0.95	0.88–1.02	0.2
Hospital characteristics			
Quintile of yearly hip fracture surgery volume highest	Reference		
4	1.10	1.01–1.20	0.02
3	1.09	0.97–1.22	0.2
2	1.12	1.00–1.25	0.06
Lowest	1.20	1.07–1.35	0.003
Teaching hospital (*vs.* not)	0.89	0.81–0.98	0.02

*The main exposure is provided as a regression coefficient because the proportion of NA use was log-transformed and cannot be directly interpreted as a hazard ratio.

ACE-I/ARB = angiotensin converting enzyme inhibitor/angiotensin receptor blocker; ASA = American Society of Anesthesiologists; HOMR = Hospital-patient One-year Mortality Risk; LOS = length of stay; NA = neuraxial anesthetic.
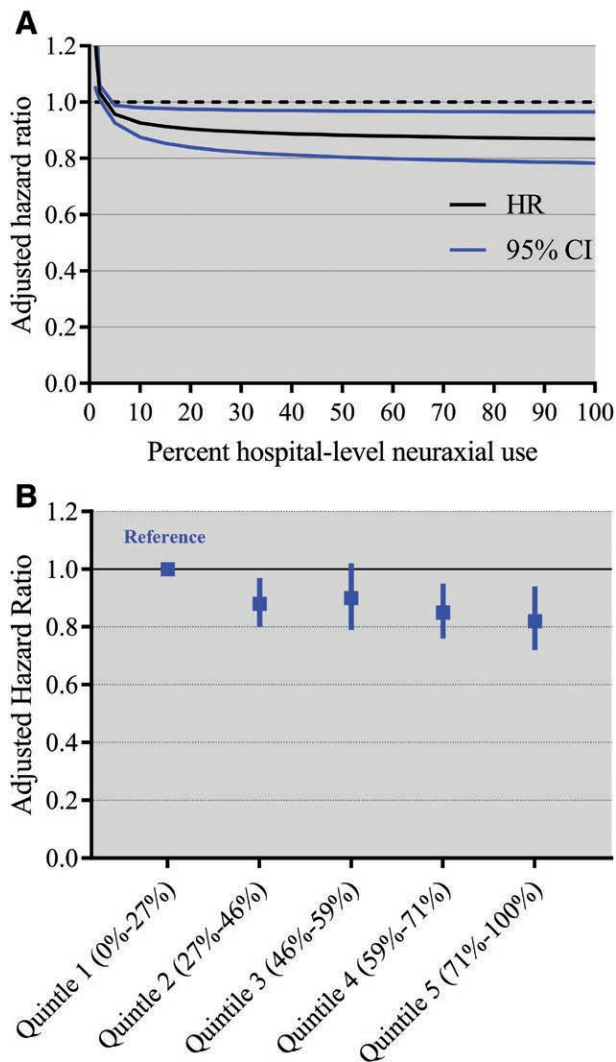
Fig. 2. The association of hospital-level neuraxial anesthesia use proportion with 30-day survival. (*A*) The log-transformed association is provided. For each value between 1 to 100%, we calculated the specific hazard ratio (HR) and 95% CI to make interpretation of the association between our log-transformed exposure with survival possible on the more familiar HR scale. The regression coefficient for the log-transformed proportion is not directly interpretable as a HR without accounting for the data transformation. The *dotted line* represents the null value for the HR (*i.e.*, a value of 1). (*B*) The HR and 95% CI within each quintile of hospital-level NA use are provided. Where the HR and 95% CI exclude 1 (the null value), the difference is statistically significant.

In our *post hoc* analysis limited to NA-only patients, the effect size increased (*P* = 0.002, regression coefficient = –0.099) relative to the full cohort. In the analysis limited to GA-only patients, the effect size decreased slightly but continued to be statistically significant (*P* = 0.002, regression coefficient = –0.084). Adding average surgical time to the model attenuated the effect size for the log of hospital-level NA use, although it remained statistically significant (*P* < 0.001, regression coefficient –0.0692).

Patient-level NA Use and Outcomes

Independent of potential confounders, including the proportion of NA use at each hospital, there was no difference in survival based on the type of anesthetic the patient received (adjusted HR for patient-level NA *versus* GA = 0.97, 95% CI, 0.93 to 1.02; *P* = 0.3) or time to discharge (adjusted HR 1.02, 95% CI, 1.00 to 1.04; *P* = 0.06). Patients who received NA had lower costs of care within 30 days of surgery (adjusted incidence rate ratio = 0.98, 95% CI, 0.97 to 0.99; *P* < 0.0001).

Perioperative Process Measures

When we compared the proportion of patients receiving certain perioperative processes of care between the lowest quintiles of NA-utilization hospitals, we did not detect any consistent trends that would suggest that the differences in postoperative survival that we found were attributable to non-anesthesia type practice variation reasons (table 3).

Discussion

In this population-based study of hospital-level variation in NA use for emergency hip fracture surgery, we found that low rates of hospital-level NA use, in particular less than 20 to 25%, were associated with decreased survival, independent of the anesthesia type received by individual patients. The proportion of hospital-level NA utilization was not associated with LOS or hospital costs. As in previous studies, we found tremendous variation in between-hospital NA use. The mechanisms underlying our findings have not been elucidated; however, our data suggest that it may be a combination of improved unmeasured perioperative processes in higher-NA-use hospitals, as well as improved NA-specific outcomes in higher-use centers. Prospective study of anesthesia-type variation is warranted to determine mechanisms to support needed improvements in hip fracture surgery survival.

Variation in the provision of medical care is associated with adverse outcomes in a number of settings.[36,37] Wijeysundera *et al.*[13] found that variation in the hospital-level utilization of preoperative medical consultations was associated with postoperative mortality. For patients having hip fracture surgery, despite the well documented variations in choice of anesthesia technique, the association of practice variation with outcomes has not been previously described. The current study adds to the perioperative practice variation literature by demonstrating that avoidance of low hospital-level NA-utilization is associated with a significant increase in postoperative survival. Our findings also provide insight into how hospital-level variation could partly explain the divergence of findings between observational studies with respect to the association of anesthesia type on hip fracture surgery outcomes. Recent studies that have not found an association between anesthesia type and mortality have accounted for the hierarchal nature of health data (*i.e.*, patients clustered within hospitals),[5,7] whereas studies

Table 3. Processes of Perioperative Care at Low *versus* High NA Utilization Hospitals

Intervention or Process	Code and Data Source	Lowest NA Use Quintile, %	Quintile 2, %	Quintile 3, %	Quintile 4, %	Highest NA Use Quintile, %
Inpatient anesthesiology consultation	OHIP: A/C015 or A/C016 after admission before surgery date	18.7	8.6	16.1	12.8	8.6
Perioperative geriatric medicine consultation	OHIP: A/C075, A/C076, A/C775, A/C770 during admission	8.7	1.9	5.6	1.9	1.9
Perioperative internal medicine consultation	OHIP: A/C135, A/C136 during admission	16.7	10.8	6.3	10.3	10.8
Preoperative LOS more than 2 days	DAD: surgery date-admission date	10.4	7.2	7.0	7.4	7.2
Nerve block	OHIP G260, G060	5.1	8.2	15.0	9.5	8.2

DAD = Discharge Abstract Database; LOS = length of stay; NA = neuraxial anesthesia; OHIP = Ontario Health Insurance Plan.

that have not adjusted for clustering have reported a survival advantage with NA.[38] While eliminating all variation in the provision of anesthesia care for hip fracture patients would be impractical and unsuitable, limiting variation to an extent attributable to indicated patient and surgical considerations may improve outcomes. Therefore, an understanding of this phenomenon is needed to improve the care and outcomes of hip fracture patients.

One could postulate that the association between increasing hospital-level NA-use and improved survival is simply an effect anesthesia type and that because more patients receive NA at high-use hospitals, it is the patient-level benefit of NA that leads to our findings. This does not appear to be the case. First, we controlled for patient-level receipt of NA in all adjusted models; therefore our finding was independent of the actual anesthesia type that each patient received. Although population-based studies provide heterogeneous findings regarding the association of NA with outcomes after hip fracture surgery,[1,4,5,7] our measures of association of NA on outcomes at the patient level (no difference in mortality, a small or no decrease in LOS) are consistent with the lowest risk of bias population-based studies.[5,7] Furthermore, a recent Cochrane review of randomized trials found no difference in the rate of mortality or major complications between anesthesia techniques for hip fracture surgery.[3] Therefore, we must consider whether there is a causal relationship between variation in hospital-level NA utilization and survival, whether this measure is simply a proxy for some unmeasured process in high-NA-use hospitals, and whether both mechanisms may contribute.

Across our primary and sensitivity analyses, increasing use of hospital-level NA was significantly associated with improved survival. Our primary analysis demonstrated a 13% relative increase in survival from 0 to 100% NA-use hospitals. However, as demonstrated in figure 2, most of the decrease in survival occurred with less than 20 to 25% NA use. This suggests that the majority of the risk associated with anesthesia-type variation is likely concentrated in hospitals that use almost no NA. Prespecified sensitivity analyses supported the association; a quintile-based analysis

found that in all but one quintile, survival increased as NA-use increased, but again, the largest improvement in survival occurred between the lowest use quintiles (0 to 27% NA use *vs.* 27 to 46% NA use, a relative drop of 12%). The linear association between increased NA use and improved survival does suggest that there may be incremental benefit in increasing NA use even in moderate use hospitals, but as a secondary analysis and relatively small effect size, this does not appear to be as robust a target. Furthermore, even this linear analysis may be heavily influenced by the significant improvement in survival in the transition from very low NA-use hospitals. Based on these analyses, we can conclude that in our healthcare system, there is a significant and consistent directional association between increased hospital-level NA use and improved survival that could support causality. However, these findings alone are insufficient to prove causation.

If a causal relationship does exist, a biologically plausible explanation is required. Our subgroup analyses restricted to NA-only and GA-only cohorts demonstrate that survival is improved to a greater degree in people who received NA in a higher-NA-use hospital. Therefore, we hypothesize that it is possible that anesthesiologists in higher-NA-use hospitals may be more facile at providing NA. Recent audits from the United Kingdom suggest that at the patient level, the choice of anesthesia type may not impact outcomes as much as how well hemodynamic goals, such as avoidance of hypotension, are met.[12] Perhaps anesthesiologists who provide NA more often are better at maintaining hemodynamic stability (or other important anesthetic goals such as appropriate sedation levels or opioid-sparing analgesia) in patients who receive NA.

However, the persistence of a significant effect of hospital-level NA use on survival even in those who received a GA suggests involvement of another mechanism. The association between hospital-level NA use and survival could be a proxy for the underlying quality of care provided at higher NA utilization hospitals. It is plausible that higher-NA-use hospitals have also standardized other aspects of perioperative care or have implemented evidence-based pathways and guideline-based

489

McIsaac *et al*.

recommendations more effectively to enhance care and outcomes. In our data, measurable interventions and processes that could contribute to improved mortality were not consistently applied in higher proportions as the use of NA increased. For example, multidisciplinary consultations were more frequently employed in low NA use hospitals. Although this could reflect higher surgeon expertise in managing perioperative care of hip fracture patients at high-NA-use hospitals, this possibility cannot be proven or disproven in our data. High-NA-use hospitals were more likely to provide nerve blocks, which many guidelines recommend; however, a 3% increase in the provision of peripheral nerve blocks is unlikely to translate into a significant increase in survival. Although shorter waits for surgery, which patients at high-NA-use hospitals had, may improve mortality rates, our models accounted for preoperative wait time. These findings do not, however, rule out the existence of underlying process differences. Administrative data have known limitations; such data do not capture all processes of care and, importantly, cannot measure the quality or appropriateness of interventions or processes applied to patient care. Therefore, future prospective research is needed to evaluate care processes in high-NA-use hospitals to identify areas of improvement that could improve survival in the high-risk population of older patients having hip facture surgery.

Strengths and Limitations

This study features several strengths. We used population-level data generated from a universal healthcare system; therefore, our results may be generalizable to similar health systems. We defined our cohort using procedural codes that are known to be accurate, and our primary outcome of death was captured from the gold standard source for mortality data in Ontario. We also preregistered our study protocol, which limits the risk of multiple outcome testing and should decrease risk of type I error. Our findings were also consistent in sensitivity analyses, including different representations of our primary exposure variable, and all analyses accounted for the hierarchal nature of our data by clustering patients in hospitals.

Limitations must also be considered. This observational study cannot prove a causal association and utilized data that was not initially collected for research purposes. We did not perform analyses of how anesthesia-type variation may interact with specific patient subgroups who may benefit most from NA (such as people with significant respiratory disease); therefore we cannot demonstrate whether our results are biased by variations in care of these higher risk patients. Rates of NA use for hip fracture surgery appear to be higher in Canada than in the United States, so future studies will be needed to identify whether our findings generalize to jurisdictions with different healthcare systems and practice patterns. As an observational study, our findings are at risk for a number of biases and in particular indication bias. Although we controlled for many patient, physician, and hospital-level factors to adjust for the indication for being at a high-NA-utilization center, our data did not contain granular patient-level data that may have

influenced the choice of hospital or anesthesia type for certain patients such as laboratory data or physiologic measures. Additionally, our regression-based analysis is not the only way that the effect of practice variation on outcomes can be evaluated. Evaluation of the concordance of the actual treatment received by each patient with the risk-adjusted, model-based preferred treatment could also have been employed.[39]

Conclusions

Hospitals that utilize a low proportion of neuraxial anesthesia for emergency hip fracture surgery have decreased rates of risk-adjusted postoperative survival. Although the underlying mechanism remains to be determined, our data suggest that it may be influenced both by mechanisms specific to provision of NA and by other underlying improved processes in higher-NA-use centers; prospective study of this phenomenon is warranted. Our findings also highlight the need to consider additional instances of practice variation in perioperative medicine and the need for observational studies to account for the hierarchal nature of health administrative data.

Research Support

Competing Interests

Correspondence

Address correspondence to Dr. McIsaac: Ottawa Hospital, 1053 Carling Avenue, Ottawa, Ontario K1Y 4E9, Canada. dmcisaac@toh.ca. This article may be accessed for personal use at no charge through the Journal Web site, www.anesthesiology.org.

References

1. Radcliff TA, Henderson WG, Stoner TJ, Khuri SF, Dohm M, Hutt E: Patient risk factors, operative care, and outcomes among older community-dwelling male veterans with hip fracture. J Bone Joint Surg Am 2008; 90:34–42
2. Neuman MD, Silber JH, Magaziner JS, Passarella MA, Mehta S, Werner RM: Survival and functional outcomes after hip fracture among nursing home residents. JAMA Intern Med 2014; 174:1273–80
3. 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, UK, John Wiley & Sons, Ltd., 2016

4. Neuman MD, Silber JH, Elkassabany NM, Ludwig JM, Fleisher LA: Comparative effectiveness of regional versus general anesthesia for hip fracture surgery in adults. ANESTHESIOLOGY 2012; 117:72–92

5. 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

6. Nordström P, Gustafson Y, Michaëlsson K, Nordström A: Length of hospital stay after hip fracture and short term risk of death after discharge: A total cohort study in Sweden. BMJ 2015; 350:h696

7. Patorno E, Neuman MD, Schneeweiss S, Mogun H, Bateman BT: Comparative safety of anesthetic type for hip fracture surgery in adults: Retrospective cohort study. BMJ 2014; 348:g4022

8. Quality-based Procedures Clinical Handbook for Hip Fractures. Toronto, Canada 2013. Available at: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/clinical-handbooks. Accessed May 30, 2016

9. Mak JC, Cameron ID, March LM; National Health and Medical Research Council: Evidence-based guidelines for the management of hip fractures in older persons: An update. Med J Aust 2010; 192:37–41

10. Management of Hip Fracture in Older People. National Clinical Guideline 111. Edinburgh, UK, 2009. Available at: http://www.sign.ac.uk/assets/sign111.pdf. Accessed May 30, 2016

11. Griffiths R, Alper J, Beckingsale A, Goldhill D, Heyburn G, Holloway J, Leaper E, Parker M, Ridgway S, White S, Wiese M, Wilson I: Management of proximal femoral fractures 2011. Anaesthesia 2011; 67:85–98

12. National Hip Fracture Database: Anaesthesia Sprint Audit of Practice. London, UK, 2014. Available at: https://www.aagbi.org/sites/default/files/NHFD anaesthestic report.pdf. Accessed May 30, 2016

13. Wijeysundera DN, Austin PC, Beattie WS, Hux JE, Laupacis A: Variation in the practice of preoperative medical consultation for major elective noncardiac surgery: A population-based study. ANESTHESIOLOGY 2012; 116:25–34

14. White SM, Griffiths R, Moppett IK: Standardising anaesthesia for hip fracture surgery. Anaesthesia 2016; 71:1391–5

15. Corallo AN, Croxford R, Goodman DC, Bryan EL, Srivastava D, Stukel TA: A systematic review of medical practice variation in OECD countries. Health Policy 2014; 114:5–14

16. Vision and Mandate. Canadian Institute of Health Information. Available at: http://www.cihi.ca/CIHI-ext-portal/internet/EN/SubTheme/about+cihi/vision+and+mandate/cihi010703. Accessed May 30, 2016

17. About Us. Institute for Clinical and Evaluative Sciences. Available at: https://www.ices.on.ca/About-ICES.aspx. Accessed May 30, 2016

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

19. 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

20. Technical Note: Wait Time for Hip Fracture Surgery Technical Note. Ottawa, Canada. Available at: http://indicatorlibrary.cihi.ca/display/HSPIL/Hip+Fracture+Surgery+Within+48+Hours. Accessed May 30, 2016

21. 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 Canadian Institute for Health Information Discharge Abstract Database, 2006

22. Richards J, Brown A, Homan C: The Data Quality Study of the Canadian Discharge Abstract Database. Proc Stat Canada Symp, 2001. Available at: http://www.statcan.gc.ca/access_acces/alternative_alternatif.action?l=eng&loc=2001001/session16/6282-eng.pdf. Accessed September 27, 2017

23. Kulkarni GS, Laupacis A, Urbach DR, Fleshner NE, Austin PC: Varied definitions of hospital volume did not alter the conclusions of volume-outcome analyses. J Clin Epidemiol 2009; 62:400–7

24. Adler R, Feldman R, eds.: A Practical Guide to Heavy Tails: Statistical Techniques and Applications. Switzerland, Birkhauser, 1998

25. Altman DG: The cost of dichotomising continuous variables. BMJ 2006; 332:1080

26. Sauerbrei W, Meier-Hirmer C, Benner A, Royston P: Multivariable regression model building by using fractional polynomials: Description of SAS, STATA and R programs. Comput Stat Data Anal 2006; 50:3464–85

27. Wodchis W, Bushmeneva K, Nikitovic M, McKillop I: Guidelines on Person-Level Costing Using Administrative Databases in Ontario. Toronto, Canada, Health System Performance Research Network, 2013. Available at: http://www.hsprn.ca/uploads/files/Guidelines_on_PersonLevel_Costing_May_2013.pdf. Accessed May 30, 2016

28. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, Saunders LD, Beck CA, Feasby TA, Ghali W: Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care. 2005; 43:1130–9. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16224307. Accessed November 18, 2012

29. van Walraven C, 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

30. Bottomley C, Kirby MJ, Lindsay SW, Alexander N: Can the buck always be passed to the highest level of clustering? BMC Med Res Methodol 2016; 16:29

31. Bilimoria KY, Liu Y, Paruch JL, Zhou L, Kmiecik TE, Ko CY, Cohen ME: Development and evaluation of the universal ACS NSQIP surgical risk calculator: A decision aid and informed consent tool for patients and surgeons. J Am Coll Surg 2013; 217:833–42.e1–3

32. van Walraven C: The Hospital-patient One-year Mortality Risk score accurately predicted long-term death risk in hospitalized patients. J Clin Epidemiol 2014; 67:1025–34

33. Fine JP, Gray RJ: A proportional hazards model for the subdistribution of a competing risk. J Am Stat Assoc 1999; 94:496

34. Austin PC, Ghali WA, Tu JV: A comparison of several regression models for analysing cost of CABG surgery. Stat Med 2003; 22:2799–815

35. Redelmeier DA, Thiruchelvam D, Daneman N: Introducing a methodology for estimating duration of surgery in health services research. J Clin Epidemiol 2008; 61:882–9

36. Dalton JE, Zidar DA, Udeh BL, Patel MR, Schold JD, Dawson NV: Practice variation among hospitals in revascularization therapy and its association with procedure-related mortality. Med Care 2016; 54:623–31

37. Giugliano RP, Camargo CA, Lloyd-Jones DM, Zagrodsky JD, Alexis JD, Eagle KA, Fuster V, O'Donnell CJ: Elderly patients receive less aggressive medical and invasive management of unstable angina. Arch Intern Med 1998;158:1113

38. Chu CC, Weng SF, Chen KT, Chien CC, Shieh JP, Chen JY, Wang JJ: Propensity score-matched comparison of postoperative adverse outcomes between geriatric patients given a general or a neuraxial anesthetic for hip surgery: A population-based study. ANESTHESIOLOGY 2015; 123:136–47

39. Dalton JE, Dawson NV, Sessler DI, Schold JD, Love TE, Kattan MW: Empirical treatment effectiveness models for binary outcomes. Med Decis Making 2016; 36:101–14