ANESTHESIOLOGY

Persistent Postoperative Opioid Prescription Fulfillment and Peripheral Nerve Blocks for Ambulatory Shoulder Surgery: A Retrospective Cohort Study

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Peripheral nerve blocks for ambulatory shoulder surgery reduce early postoperative pain
- Persistent opioid prescription fulfillment after ambulatory shoulder surgery is common, with more than 10% of previously opioid-naive patients still requiring opioid prescriptions 180 days after surgery

What This Article Tells Us That Is New

- Among 48,523 patients undergoing ambulatory shoulder surgery in Ontario, Canada, between 2012 and 2017, 16% of patients receiving a nerve block and 17% of patients without a nerve block went on to demonstrate persistent postoperative opioid prescription fulfillment
- This statistically significant difference has questionable clinical significance, and was not reproduced in a variety of sensitivity analyses
- There is no consistent association between the receipt of a peripheral nerve block and a lower risk of persistent opioid prescription fulfillment after ambulatory shoulder surgery

ABSTRACT

Background: There is need to identify perioperative interventions that decrease chronic opioid use. The authors hypothesized that receipt of a peripheral nerve block would be associated with a lower incidence of persistent postoperative opioid prescription fulfillment.

Methods: This was a retrospective population-based cohort study examining ambulatory shoulder surgery patients in Ontario, Canada. The main outcome measure was persistent postoperative opioid prescription fulfillment. In opioid-naive patients (no opioid prescription fulfillment in 90 days preoperatively), this was present if an individual fulfilled an opioid prescription of at least a 60-day supply during postoperative days 90 to 365. In opioid-exposed (less than 60 mg oral morphine equivalent dose per day within 90 days preoperatively) or opioid-tolerant (60 mg oral morphine equivalent dose per day or above within 90 days preoperatively) patients, this was classified as present if an individual experienced any increase in opioid prescription fulfillment from postoperative day 90 to 365 relative to their baseline use before surgery. The authors' exposure was the receipt of a peripheral nerve block.

Results: The authors identified 48,523 people who underwent elective shoulder surgery from July 1, 2012, to December 31, 2017, at one of 118 Ontario hospitals. There were 8,229 (17%) patients who had persistent postoperative opioid prescription fulfillment. Of those who received a peripheral nerve block, 5,008 (16%) went on to persistent postoperative opioid prescription fulfillment compared to 3,221 (18%) patients who did not (adjusted odds ratio, 0.90; 95% CI, 0.83 to 0.97; $P = 0.007$). This statistically significant observation was not reproduced in a coarsened exact matching sensitivity analysis (adjusted odds ratio, 0.85; 95% CI, 0.71 to 1.02; $P = 0.087$) or several other subgroup and sensitivity analyses.

Conclusions: This retrospective analysis found no association between receipt of a peripheral nerve block and a lower incidence of persistent postoperative opioid prescription fulfillment in ambulatory shoulder surgery patients.

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Chronic opioid use has resulted in serious morbidity, mortality, and economic cost.[1,2] Recent publications clearly identify that opioid prescriptions from acute care visits contribute to chronic opioid use.[3,4] Specifically, prescribing opioids at hospital discharge to opioid-naive patients may increase the odds of chronic opioid use 1 yr after discharge fivefold.[5] This is of particular concern in the perioperative population, as several studies demonstrate that surgery is associated with an increased risk of persistent postoperative opioid utilization.[6,7] Depending on the definition of persistent postoperative opioid utilization

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used and the surgical population studied, the incidence of persistent opioid use after elective surgery varies widely.[6,8] Given concerns related to persistent opioid use in surgical patients, there is a need to identify perioperative interventions that can decrease risks related to postoperative opioid prescribing and chronic opioid use.

Ambulatory orthopedic surgery is common, and variations in perioperative anesthetic and analgesic care for orthopedic patients is well documented. Shoulder surgery is one of the most painful ambulatory surgeries commonly performed and is associated with a threefold increase in unplanned hospital admissions compared with other common orthopedic procedures.[9,10] Peripheral nerve blocks (*e.g.*, local anesthetic injected around a specific nerve bundle) reduce early postoperative pain to a clinically important extent; however, the proportion of patients who receive peripheral nerve blocks in elective shoulder surgery is variable (15 to 52%).[11–13] This may be due to a variety of factors, including a lack of equipment and expertise in some centers, as well as substantial uncertainty about the medium- and long-term effects of peripheral nerve blocks in shoulder surgery.[14] To our knowledge, there has been one study that has examined peripheral nerve blocks and persistent opioid use in ambulatory shoulder surgery.[15] Mueller *et al.*[15] found no association between persistent opioid use and the receipt of a peripheral nerve block in patients undergoing shoulder arthroplasty, but this study used unvalidated billing codes in a homogenous population of patients with private health insurance (*i.e.*, age less than 65 yr). Despite guidelines that recommend use of peripheral nerve blocks to reduce postoperative opioid use, whether improved early analgesia with peripheral nerve blocks results in lower rates of persistent opioid use is unknown due to the paucity of evidence in this area.[16,17]

Given the lack of evidence, and the important public health implications, our primary objective was to estimate the population-level association between peripheral nerve blocks and persistent postoperative opioid prescription fulfillment in the first postoperative year after ambulatory shoulder surgery. We hypothesized that the receipt of a peripheral nerve block would be associated with a lower incidence of persistent postoperative opioid prescription fulfillment among patients undergoing ambulatory surgery. Our secondary objective was to evaluate whether the degree of preoperative opioid prescription fulfillment modified the association between receipt of peripheral nerve block and persistent postoperative opioid prescription fulfillment.

Materials and Methods

Study Design, Setting, and Data Sources

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 (Toronto, Ontario, Canada), an independent research institute. Datasets used for the study included the Same Day Surgery Database, which captures all planned ambulatory surgeries; the Discharge Abstract Database, which captures all inpatient hospitalizations; the Ontario Health Insurance Plan 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 Narcotic Monitoring System, which captures all prescription opioid drug claims for Ontario residents; and the ICES Physician Database, which houses information on physician specialty, demographics, training, and workload. Because data used for this study were routinely collected and deidentified, it was legally exempt from research ethics review.

Participants

We identified all Ontario residents aged 18 yr and older who underwent elective ambulatory shoulder surgery. Participants were identified using the Same Day Surgery Database through application of previously studied Canadian Classification of Interventions codes to identify the following shoulder surgeries: shoulder arthroscopy, arthroplasty synthetic repair, implantation of internal device shoulder joint, repair of recurrent dislocation, other shoulder repair, shoulder arthrotomy, division of joint capsule, lining or cartilage shoulder, synovectomy shoulder, other local excision or destruction of shoulder joint, and other excision of joint (shoulder). The study period extended from July 1, 2012, to December 31, 2017 (latest complete data at the time of cohort creation), and we created a patient-level analytic data set by including only the first surgery for any participant in the study period. The start time was chosen to coincide with the introduction of the Narcotic Monitoring System tracking system for opioid use in Ontario.

Given the important postulated role of preoperative opioid use, we defined preoperative utilization using modified preoperative "O-NET" opioid exposure criteria (opioid-naive [N], no history of opioid use in the 90 days before surgery; opioid-exposed [E], any opioid exposure less than 60 mg morphine equivalent dose per day within 90 days preoperatively; opioid-tolerant [T], a dose of 60 mg morphine equivalent dose per day or above in the 90 days before surgery).[6] We modified the time frame of the opioid tolerant definition timeframe in the consensus guideline from 7 days to 90 days (1) to ensure a discrete and mutually exclusive definition and (2) to avoid misclassification of patients who did not fill a prescription in the 7 days before the surgery, but were still prescribed a greater than 60 mg morphine daily dose. The morphine equivalent dose per day was calculated by taking the sum total of opioid prescriptions filled during the 90-day time frame, converting to oral morphine equivalents, and

dividing the sum total oral morphine equivalents by the number of days (*e.g.*, 90 days).

Exposure

We identified peripheral nerve blocks on the day of surgery through use of validated Ontario Health Insurance Plan physician billing codes (G260-major plexus block, G060-major nerve block, G061-minor nerve block, or G279-percutaneous nerve block catheter for continuous infusion analgesia), which 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 blocks.[14]

Outcomes

Our primary outcome was persistent postoperative opioid prescription fulfillment, with data obtained from the Narcotic Monitoring System. The actual consumption of opioids prescribed is not captured in our dataset. We defined persistent postoperative opioid prescription fulfillment using recently published consensus guidelines.[6] Specifically, for opioid-naive patients, persistent postoperative opioid prescription fulfillment was classified as a fulfillment of an opioid prescription if an individual fulfilled an opioid prescription of at least a 60-day supply during postoperative days 90 to 365. For preoperative opioid-exposed or -tolerant individuals, persistent postoperative opioid prescription fulfillment is classified as a fulfillment of an opioid prescription if an individual experienced any increase in opioid prescription fulfillment from postoperative days 90 to 365 relative to their baseline use in the 90 days before surgery.[6] This was operationalized by comparing (A) the mean daily morphine equivalents in the 90 days before the surgery to (B) the mean daily morphine equivalent in day 90 to 360 after surgery. If B was greater than A, we would record the patient as having persistent postoperative opioid prescription fulfillment. Our secondary outcomes were fulfillment of any postoperative opioid prescription within 14 days of the index surgery (a binary variable), the quantity of opioids prescribed (oral morphine equivalents in milligrams per day) within 14 days of surgery,[18] and the total quantity of opioids prescribed in the year after surgery (oral morphine equivalents in milligrams per day). These secondary outcomes were also captured from the Narcotic Monitoring System.

Covariates

Patient demographics, comorbidities, preoperative opioid prescription fulfillment, and preoperative patterns of healthcare resource use are likely to confound the association between the receipt of a peripheral nerve block and persistent opioid prescription fulfillment. Therefore, we obtained detailed baseline data on all participants, including age; sex; rural (*vs.* urban) residence; socioeconomic status; American Society of Anesthesiologists (Schaumburg, Illinois) Physical Status score; baseline 1-yr mortality risk using the Johns Hopkins Adjusted Clinical Groups score (which demonstrates excellent discrimination [c-statistic 0.92] and calibration)[19]; baseline acute care utilization patterns (number of acute care hospitalizations and number of emergency department visits in the year before surgery); and predicted healthcare utilization based on the Adjusted Clinical Groups Resource Utilization Band,[20] which accounts for patterns of preoperative inpatient and outpatient health resource use. For specific patient comorbidities, we used validated measures identifying a history of asthma,[21] chronic obstructive pulmonary disease,[22] diabetes mellitus,[23] acute coronary syndrome,[24] heart failure,[25] and hypertension.[26] Elixhauser comorbidities[27] were used for all other comorbidities without validated measures.

Sample Size

This was a population-based study; therefore, we included all eligible members of the Ontario population. No formal statistical power calculation was conducted.

Missing Data

Data were missing for 0.1% of participants for the covariate rural *versus* urban residence, 0.21% of participants for the covariate neighborhood income, and 7.0% of institutional data (hospitals). We imputed these covariates with the central measure of tendency (for neighborhood income third) or most common value (for rural *vs.* urban residence). For missing institution, we inputted a missing value (*e.g.*, 9,999) so that patients with a missing institution would be clustered together. We then conducted a sensitivity analysis in our cohort without the imputed institution to see if our imputation assumption impacted the results.

Statistical Analysis

The study protocol was registered with the Center for Open Science (Charlottesville, Virginia; registration DOI: 10.17605/OSF.IO/R65N7), and our full analytic plan was determined *a priori*. The dataset was created, manipulated, and analyzed using Stata version 15.1 (StataCorp LLC, USA). Baseline covariate data were 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.[28]

To estimate the association of receipt of peripheral nerve blocks with the likelihood of persistent opioid prescription fulfillment, we calculated unadjusted and adjusted effect measures. Our primary approach to adjusted analyses was to use multivariable regression models that accounted for clustering of individuals within hospitals (the highest level in our data hierarchy) using generalized estimating

equation methods. Adjusted regression models included the exposure of interest (peripheral nerve block; binary), as well as preoperative opioid prescription fulfillment (categorical; naive, exposed, or tolerant), age (restricted cubic spline with five knots), sex (binary), neighborhood income quintile (five-level categorical variable), rurality (binary), surgical procedure and technique (categorical; full seven-digit Canadian Classification of Interventions classification), anesthetic (binary; general anesthesia *vs.* sedation), asthma (binary), chronic obstructive pulmonary disease (binary), diabetes mellitus (binary), acute coronary syndrome binary (binary), heart failure (binary), hypertension (binary), each Elixhauser comorbidity (binary), year of surgery (six-level categorical), resource utilization band (six-level categorical), baseline 1-year mortality risk using the Johns Hopkins Adjusted Clinical Groups score (linear, as in its derivation),[19] previous acute hospitalizations (binary), and previous emergency department visits (binary). As per our protocol, we attempted to use a log binomial model as the incidence of our outcome was greater than 10%, but our model did not converge, so we moved to a logistic regression framework to generate adjusted odds ratios.[29]

For our secondary outcomes, the analysis of initial fulfillment of a postoperative opioid prescription between the two dichotomous peripheral nerve block exposure levels (yes/no) was conducted in the same manner as the primary analysis. The continuous outcome of oral morphine equivalents initially prescribed and over the first year was analyzed using linear regression. Since there was significant dispersion of the oral morphine equivalents data (right-skewed distribution), as per protocol, we went on to analyze oral morphine equivalents using negative binomial regression adjusting for the same covariates as the primary analysis.

Sensitivity Analysis

To test the robustness of our primary analysis, we utilized an analysis based on matching (as opposed to regression) to control for confounders. Specifically, we used coarsened exact matching, a type of monotonic imbalance bounding used to preprocess the data to create two groups (peripheral nerve block *vs.* no peripheral nerve block) that are identical within coarsened ranges of each variable. Compared to propensity score matching, which matches individuals on average across covariates, coarsened exact matching is less model-dependent and lowers bias (by removing heterogeneity)[30] as it requires fewer assumptions (such as proper specification of the propensity score model).[31] Our coarsened exact matching model matched on all covariates that were included in our primary regression analysis, including an exact match on hospital. It was conducted in a 1:many matching method per defined methods.[30] See Supplemental Digital Content 1 (http://links.lww.com/ALN/C677) for a full description of coarsening, including the formal prespecification of the matching in the model. The matched cohort was then analyzed using a logistic regression framework to generate adjusted odds ratios. Adjusted absolute risk differences and adjusted number needed to treat values with 95% CI were also calculated based on the coarsened exact matching matched cohort.

Subgroup Analyses

The primary model was repeated within the three subgroups of preoperative opioid prescription fulfillment (naive, exposed, tolerant) to examine preoperative opioid prescription fulfillment and persistent postoperative opioid prescription fulfillment. Furthermore, we compared the subset of patients who had a continuous catheter, instead of a single shot block (recoding the exposure as a three-level categorical variable: no peripheral nerve block [reference], single shot peripheral nerve block, peripheral nerve block with catheter). We also tested for presence of effect modification by adding the multiplicative interaction terms to the primary outcome model, (1) peripheral nerve block × sex, (2) peripheral nerve block × depression, and (3) peripheral nerve block × drug abuse, as these variables are known risk factors for chronic opioid use.[6]

Post Hoc and Reviewer-requested Sensitivity Analyses

To understand the importance of our outcome definition, we conducted a *post hoc* analysis using another common definition of persistent postoperative opioid prescription fulfillment: more than 1 opioid prescription within 1 to 90 days after surgery and (a) more than 10 opioid prescriptions or (b) a 120-day supply of opioids within 91 to 365 days after surgery.[32–34] We examined the association of the receipt of peripheral nerve blocks with the likelihood of persistent opioid prescription fulfillment and calculated unadjusted and adjusted effect measures in a similar manner to our primary analysis using multivariable regression models using generalized estimating equation methods. The second definition was also examined with coarsened exact matching and analyzed using a logistic regression framework to generate adjusted odds ratios. To examine anesthetic technique, we compared the subset of patients who had sedation rather than a general anesthetic with their peripheral nerve block (recoding the exposure as a four-level categorical variable: general anesthesia [reference], peripheral nerve block and general anesthesia, peripheral nerve block and sedation, sedation and local infiltration). To examine type of shoulder surgery, we compared patients across a four-level surgery type categorical variable (total/partial arthroplasty [reference], arthroscopic procedure, open procedure, other procedure). Last, we also tested for presence of effect modification by preoperative opioid exposure status by adding the multiplicative interaction terms to the primary outcome model: (1) peripheral nerve block × opioid exposure level (naive, exposed, tolerant), and (2) peripheral nerve block catheter × opioid exposure level (naive, exposed, tolerant).

Results

We identified 48,523 people who underwent shoulder surgery from July 1, 2012, to December 31, 2017, at one of 118 Ontario hospitals. Overall, 30,377 (63%) patients received a peripheral nerve block, and 18,146 (37%) patients did not (fig. 1). Out of those who received a peripheral nerve block, 1,369 (5%) patients had a peripheral nerve block catheter placed with their surgery. Patients receiving a peripheral nerve block were similar to patients who did not; 4 of 44 measured covariates had an absolute standardized difference greater than 10 (age, rurality, type of shoulder repair, year), and one absolute standardized difference exceeded 35 (anesthetic type). Complete patient characteristics by peripheral nerve block group are provided in table 1.

Primary Outcome

In the total cohort, there were 8,229 (17%) patients who had persistent postoperative opioid prescription fulfillment. Of those that received a peripheral nerve block, 5,008 (16%) went on to have persistent postoperative opioid prescription fulfillment compared to 3,221 (18%) patients who did not receive a peripheral nerve block (unadjusted odds ratio = 0.91, 95% CI, 0.87 to 0.96; $P < 0.001$). After multilevel multivariable adjustment, there continued to be a statistically significant association between receipt of a peripheral nerve block and reduced odds of persistent postoperative opioid prescription fulfillment (adjusted odds ratio = 0.90; 95% CI, 0.83 to 0.97; $P = 0.007$). The fully adjusted regression model is presented in table 2.

Secondary Outcomes

The majority of patients (n = 45,693; 94%) filled a postoperative opioid prescription within 14 days of their index shoulder surgery. In patients who had receipt of a peripheral nerve block compared to those that did not, there was no statistically significant difference in the odds of any postoperative opioid prescription within 14 days of their surgery (adjusted odds ratio = 1.11; 95% CI, 0.92 to 1.34; $P = 0.254$).

Using linear regression, the adjusted mean difference of oral morphine equivalents prescribed between patients who did or did not receive a peripheral nerve block in the 14 days after surgery was 1 mg (95% CI, –38 to 40; $P = 0.945$). In the year after surgery (days 0 to 365), comparing patients who received a peripheral nerve block to those who did not, there was a statistically significant reduced adjusted mean difference in oral morphine equivalents (mean difference = –327 mg; 95% CI, –646 to 8; $P = 0.045$). The overall adjusted mean oral morphine equivalent in patients that did not receive a peripheral nerve block was 3,106 mg (95% CI, 2,832 to 3,381) compared to 2,728 mg (95% CI, 2,481 to 2,976) in patients who received a peripheral nerve block. As oral morphine equivalents data was right skewed, we went on to test the robustness of this finding using negative binomial regression analysis to account for overdispersion of the oral morphine equivalents. There was no statistically significant association between peripheral nerve block receipt and receipt of oral morphine equivalents in the first 14 days after surgery (adjusted relative risk = 1.02; 95% CI, 0.95 to 1.09; $P = 0.665$) or 365 days after surgery

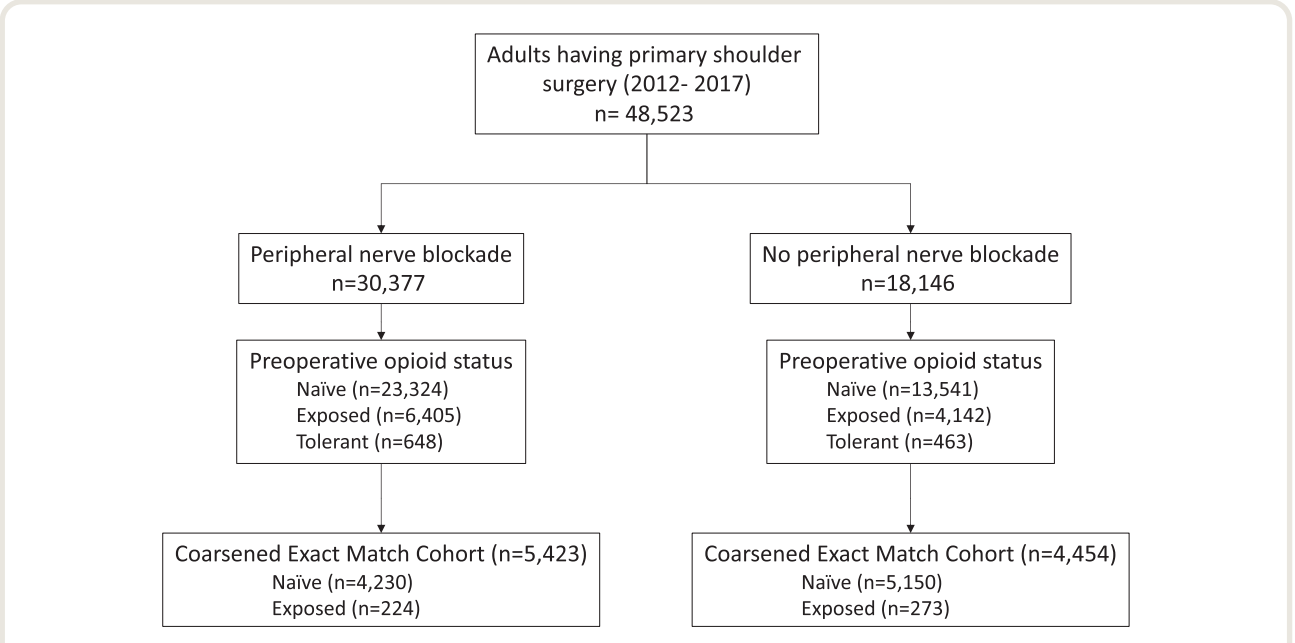

Fig. 1. Study flow diagram of the analytical dataset depicting the full cohort and the coarsened exact match analysis cohort.

between patients who did or did not receive a peripheral nerve block (adjusted relative risk = 0.99; 95% CI, 0.92 to 1.08; $P = 0.886$).

Subgroup Analyses

In our cohort, 36,865 (76%) of patients were opioid-naive, 10,547 (22%) of patients were opioid-exposed, and 1,111 (2%) of patients were opioid-tolerant. Within the opioid-naive preoperative exposure group (n = 36,865), the receipt of a peripheral nerve block was not statistically significantly associated with persistent postoperative opioid prescription fulfillment (adjusted odds ratio = 0.95; 95% CI, 0.86 to 1.04; $P = 0.266$). In the opioid-exposed group (n = 10,547), receipt of a peripheral nerve block was associated with a reduced odds of persistent postoperative opioid prescription fulfillment (adjusted odds ratio = 0.86; 95% CI, 0.77 to 0.96; $P = 0.006$), whereas the opioid tolerant group (n = 1,111) was not (adjusted odds ratio = 1.03; 95% CI, 0.78 to 1.36; $P = 0.809$; table 3).

Sensitivity Analysis

The coarsened exact match resulted in a creation of a matched cohort of 9,877 people with a peripheral nerve block, and people without a peripheral nerve block (20% of total cohort; see Supplemental Digital Content 2, http://links.lww.com/ALN/C678, for full characteristics of the coarsened exact matched cohort). Within the matched cohort, 9,380 (95%) were opioid-naive, 497 (5%) were opioid-exposed, and no patients were opioid-tolerant (due to the small sample of opioid-tolerant patients in

Table 1. Characteristics of the Study Cohort (n = 48,523)

	No Peripheral Nerve Block (n = 18,146)	Peripheral Nerve Block (n = 30,377)	Absolute Standardized Difference
	n (%)*	n (%)*	
Preoperative opioid use†			
Naive	13,541 (74.6)	23,324 (76.8)	2.6
Exposed	4,142 (22.8)	6,405 (21.1)	2.3
Tolerant	463 (2.6)	648 (2.1)	3.1
Preoperative drug use			
Benzodiazepine	1,470 (8.1)	2,441 (8.0)	0.3
Tetrahydrocannabinol	49 (0.3)	99 (0.3)	0
Demographics			
Age, yr, mean ± SD	51 ± 14)	53 ± 14)	10.4
Female	6,052 (33.4)	10,601 (34.9)	1.0
Rural	3,445 (19.0)	3,844 (12.7)	11.8
Neighborhood income quintile	2,962 (16.4)	4,586 (15.1)	2.4
1			
2	3,426 (18.9)	5,460 (18.0)	1.5
3	3,733 (20.6)	6,299 (20.7)	0.1
4	3,973 (22.0)	6,748 (22.3)	0.4
5	4,050 (22.4)	7,284 (24.0)	2.0
Anesthesia type			
General anesthesia (*vs.* sedation)	17,790 (98.0)	26,582 (87.5)	35.4
Surgery type			
Total/partial arthroplasty	101 (0.6)	233 (0.8)	2.4
Arthroscopic shoulder surgery‡	4,111 (22.7)	6,148 (20.2)	3.5
Open shoulder surgery‡	13,655 (75.3)	23,872 (78.6)	4.2
Other shoulder repair	279 (1.5)	124 (0.4)	11.1
Year of surgery			
2012	2,496 (7.3)	3,454 (11.4)	11.2
2013	3,235 (17.8)	5,075 (16.7)	1.9
2014	3,279 (18.1)	5,174 (17.0)	1.9
2015	3,192 (17.6)	5,369 (17.7)	0.2
2016	3,035 (16.7)	5,506 (18.1)	2.4
2017	2,909 (16.0)	5,799 (19.1)	5.3
Healthcare resource use			
Hospitalization in the last year	991 (5.5)	1,438 (4.7)	3.3
Emergency department visit in the last year	8,482 (46.7)	12,155 (40.0)	1.8
Resource utility band			
0	25 (0.1)	4 (0.0)	4.5
1	301 (1.7)	383 (1.3)	3.2
2	1,957 (10.8)	2,770 (9.1)	4.4
3	11,978 (66.0)	20,164 (66.4)	0.3
4	2,863 (15.8)	5,312 (17.5))	3.1
5	1,022 (5.6)	1,744 (5.7)	0.4

(*Continued*)

Table 1. (Continued)

	No Peripheral Nerve Block (n = 18,146)	Peripheral Nerve Block (n = 30,377)	Absolute Standardized Difference
	n (%)*	n (%)*	
Comorbidities			
ASA score < 3	12,118 (66.8)	19,073 (62.8)	2.5
Cerebrovascular disease	55 (0.3)	87 (0.3)	0.3
Chronic renal disease	29 (0.2)	29 (0.2)	1.8
Dialysis	13 (0.1)	16 (0.1)	0.8
Dementia	0	0	
Primary malignancy	121 (0.7)	145 (0.5)	2.5
Metastatic solid tumor	13 (0.1)	22 (0.1)	0.0
Peripheral vascular disease	27 (0.1)	64 (0.2)	1.5
History of peptic ulcer disease	23 (0.1	39 (0.1)	0.0
Liver disease	31 (0.2)	31 (0.1)	1.9
Rheumatologic disease	26 (0.1)	38 (0.1)	0.5
Hemiplegia or paraplegia	17 (0.1)	11 (0)	2.3
Atrial arrhythmia	70 (0.4)	123 (0.4)	0.3
History of venous thromboembolism	12 (0.1)	18 (0.1)	0.3
History of heart failure	246 (1.4)	404 (1.3)	0.2
History of hypertension	6,063 (33.4)	10,966 (36.1)	1.7
History of diabetes mellitus	2,640 (14.5)	4,644 (15.3)	1.5
Chronic obstructive pulmonary disease	2,292 (12.6)	3,744 (12.3)	0.7
Asthma	3,357 (18.5)	5,497 (18.1)	0.7
Myocardial infarction	309 (1.7)	558 (1.8)	1.0
Cardiac valvular disease	21 (0.1)	38 (0.1)	0.3
Disease of the pulmonary circulation	21 (0.1)	45 (0.1)	0.9
Coagulopathy	24 (0.1)	28 (0.1)	1.2
Obesity	124 (0.7)	204 (0.7)	0.1
Weight loss	10 (0.1)	4 (0.0)	2.3
Blood loss anemia	125 (0.7)	194 (0.6)	0.6
Deficiency anemia	6 (0.0)	16 (0.0)	0.9
Alcohol abuse	98 (0.5)	100 (0.3)	3.2
Drug abuse	33 (0.2)	37 (0.1)	1.5
Psychosis	4 (0.0)	8 (0.0)	0.3
Depression	58 (0.3)	110 (0.4)	0.7
Frailty	247 (1.4)	367 (1.2)	1.3

*Unless otherwise specified. †Modified O-NET criteria as opioid-naive (N), no history of opioid use in the 90 days before surgery; opioid-exposed (E), any opioid exposure less than 60 mg morphine equivalent dose per day within 90 days preoperatively; opioid-tolerant (T), a dose of 60 mg morphine equivalent dose per day or above in the 90 days before surgery. ‡Joint, ligament, or rotator cuff.

ASA, American Society of Anesthesiologists.

our full cohort). There were 487 (4.9%) patients who had persistent postoperative opioid prescription fulfillment. Within the matched cohort, the presence of a peripheral nerve block was not associated with a statistically significant decrease in the odds of persistent postoperative opioid prescription fulfillment (odds ratio = 0.85; 95% CI, 0.71 to 1.02; $P = 0.087$). Examining the coarsened exact match analysis by opioid-naive and opioid-exposed groups, we found no statistically significant difference between patients who received a peripheral nerve block compared to those who did not receive a peripheral nerve block (table 3).

In the full cohort, we compared no peripheral nerve block (reference category) *versus* single-shot peripheral nerve block and catheter peripheral nerve block. The presence of a catheter was not associated with decreased adjusted odds of persistent postoperative opioid prescription fulfillment (adjusted odds ratio = 1.00; 95% CI, 0.86 to 1.17; $P = 0.974$), whereas there was a statistically significant decreased adjusted odds of persistent postoperative opioid prescription fulfillment in the single-shot peripheral nerve block group (adjusted odds ratio = 0.90; 95% CI, 0.83 to 0.97; $P = 0.007$) compared with those who did not receive a nerve block. See table 4 for further sensitivity analyses within the opioid exposure groups. When we added our prespecified interaction terms into the model, we found that sex (interaction $P = 0.18$), depression (interaction $P = 0.21$), and drug abuse (interaction $P = 0.20$) did not significantly modify the association of peripheral nerve block with persistent postoperative opioid prescription fulfillment. We repeated our analysis excluding patients with missing hospital data (7% of the cohort excluded) and found similar differences in the adjusted odds of persistent postoperative opioid prescription fulfillment compared with our primary analysis (adjusted odds ratio = 0.91; 95% CI, 0.84 to 0.98; Supplemental Digital Content 3, http://links.lww.com/ALN/C679).

Post Hoc and Reviewer-requested Analysis

Our analysis was repeated using a second definition of persistent postoperative opioid prescription fulfillment (patients with more than 1 opioid prescription within 1 to 90 days after surgery and [a] more than 10 opioid prescriptions or [b] a 120-day supply of opioids within 91 to 365 days after surgery). Using this definition, there were 6,304 (13%) patients who had persistent postoperative opioid prescription fulfillment, and of those who received a peripheral nerve block, 3,769 (12%) went on to have persistent postoperative opioid use compared to 2,535 (14%) patients who did not receive a peripheral nerve block (adjusted odds ratio = 0.85; 95% CI, 0.78 to 0.93; $P < 0.001$) with this definition (Supplemental Digital Content 4, http://links.lww.com/ALN/C680).

The anesthetic technique and the type of surgical procedure were also examined (see table 4 with these *post hoc* reviewer-requested analyses). When we added interaction terms into the model, we found that neither preoperative opioid exposure (interaction $P = 0.33$) nor the receipt of a catheter (interaction $P = 0.18$) significantly modified the association of peripheral nerve block with persistent postoperative opioid prescription fulfillment.

Table 2. Fully Adjusted Regression Model for Risk of Persistent Postoperative Opioid Prescription Fulfillment Using the Modified Consensus Definition* in the Full Cohort

Covariate	Odds Ratio	95% CI
Peripheral nerve block (*vs.* none)	0.90	0.83–0.97
Preoperative opioid prescription fulfillment†		
Naive	Reference	
Exposed	8.0	7.3–8.8
Tolerant	9.4	8.0–11.2
Preoperative drug use		
Benzodiazepine (*vs.* none)	6.6	6.0–7.3
Tetrahydrocannabinol (*vs.* none)	7.3	4.4–12.6
Demographics		
Age linear segment		
Restricted cubic spline segment 1	1.04	1.03–1.05
Restricted cubic spline segment 2	0.96	0.93–0.98
Restricted cubic spline segment 3	1.01	0.78–1.29
Restricted cubic spline segment 4	1.36	0.81–2.31
Female (*vs.* male)	1.01	0.95–1.07
Rural (*vs.* not rural)	1.00	0.92–1.09
Neighborhood income quintile		
1 (lowest)	Reference	
2	0.93	0.85–1.02
3	0.88	0.81–0.96
4	0.84	0.76–0.93
5 (highest)	0.75	0.69–0.83
Anesthesia type		
General anesthesia (*vs.* sedation)	0.91	0.78–1.06
Surgery type		
Total/partial arthroplasty	Reference	
Arthroscopic shoulder surgery‡	1.42	0.87–2.31
Open shoulder surgery‡	1.33	0.84–2.09
Other shoulder repair	1.22	0.66–2.28
Year of surgery		
2012	Reference	
2013	0.94	0.83–1.07
2014	0.89	0.81–0.98
2015	0.84	0.75–0.94
2016	0.81	0.71–0.91
2017	0.81	0.72–0.91
Healthcare resource use		
Hospitalization in the last year (*vs.* none)	0.79	0.67–0.92
Emergency department visit in the last year (*vs.* none)	0.81	0.75–0.87
Resource utility band		
0 (Reference)	Reference	Reference
1	2.55	0.62–10.34
2	2.18	0.55–8.68
3	2.53	0.65–9.87
4	3.39	0.86–13.27
5	3.22	0.80–13.03
Comorbidities		
ASA score < 3	1.39	1.29–1.49
Cerebrovascular disease	1.53	0.98–2.39
Chronic renal disease	0.75	0.341–1.67
Dialysis	0.80	0.258–2.45
Dementia	Omitted	Omitted
Primary malignancy	0.71	0.48–1.03
Metastatic solid tumor	0.95	0.334–2.70
Peripheral vascular disease	1.15	0.63–2.10
History of peptic ulcer disease	1.04	0.53–2.05
Liver disease	0.90	0.378–2.12
Rheumatologic disease	1.16	0.57–2.36
Hemiplegia or paraplegia	0.64	0.142–2.86
Atrial arrhythmia	1.32	0.88–1.99
History of venous thromboembolism	0.76	0.26–2.27
History of heart failure	1.34	1.11–1.61
History of hypertension	1.17	1.09–1.26
History of diabetes mellitus	1.05	0.97–1.14
Chronic obstructive pulmonary disease	1.34	1.23–1.45
Asthma	1.16	1.07–1.26
Myocardial infarction	0.90	0.73–1.11
Cardiac valvular disease	0.45	0.183–1.10
Disease of the pulmonary circulation	1.04	0.52–2.06
Coagulopathy	1.37	0.66–2.83
Obesity	1.28	0.99–1.66
Weight loss	0.70	0.160–3.09
Blood loss anemia	0.90	0.64–1.26
Deficiency anemia	1.74	0.75–4.03
Alcohol abuse	0.92	0.61–1.37
Drug abuse	2.68	1.20–5.99
Psychosis	0.294	0.043–2.03
Depression	2.31	1.40–3.80
Frailty	0.89	0.70–1.12

*Persistent postoperative opioid prescription fulfillment as defined in Materials and Methods. †Modified O-NET criteria as opioid-naive (N), no history of opioid use in the 90 days before surgery; opioid-exposed (E), any opioid exposure less than 60 mg morphine equivalent dose per day within 90 days preoperatively; opioid-tolerant (T), a dose of 60 mg morphine equivalent dose per day or above in the 90 days before surgery. ‡Joint, ligament, tendon.

ASA, American Society of Anesthesiologists.

Discussion

In this retrospective, population-based cohort study examining nerve blocks in 48,523 shoulder surgery patients in

Table 3. Association of Peripheral Nerve Blocks with Persistent Postoperative Opioid Prescription Fulfillment* in Ambulatory Shoulder Surgery

	Persistent Postoperative Opioid, n (%)	No Peripheral Nerve Block		Peripheral Nerve Block		Unadjusted Odds Ratio (95% CI)	*P* Value	Adjusted† Odds Ratio (95% CI)	*P* Value
		Total, n	Persistent Postoperative Opioid, n (%)	Total, n	Persistent Postoperative Opioid, n (%)				
Primary analysis									
Full cohort, n = 48,523	8,229 (17.0)	18,146	3,221 (17.8)	30,377	5,008 (16.5)	0.91 (0.87–0.96)	< 0.001	0.90 (0.83–0.97)	0.007
Preoperative opioid use									
Naive, n = 36,865	2,862 (7.8)	13,541	1,054 (7.8)	23,324	1,808 (8.4)	1.00 (0.92–1.08)	0.912	0.95 (0.86–1.04)	0.266
Exposed, n = 10,547	4,690 (44.5)	4,142	1,890 (45.6)	6,405	2,800 (43.7)	0.93 (0.86–1.00)	0.053	0.86 (0.77–0.96)	0.006
Tolerant, n = 1,111	677 (60.9)	463	277 (59.8)	648	400 (61.7)	1.08 (0.85–1.38)	0.522	1.03 (0.78–1.36)	0.809
Sensitivity analysis (coarsened exact matching)									
Full cohort, n = 9,877	487 (4.9)	4,454	237 (5.3)	5,423	250 (4.6)	Not applicable	Not applicable	0.85 (0.71–1.02)	0.087
Preoperative opioid use								0.84 (0.67–1.05)	
Naive, n = 9,380	309 (3.3)	4,230	152 (3.6)	5,150	157 (3.0)	Not applicable	Not applicable	0.85 (0.59–1.23)	0.130
Exposed, n = 497	118 (23.7)	224	85 (37.9)	273	93 (34.1)	Not applicable	Not applicable		0.394

P < 0.05 is statistically significant.
*Consensus definition of persistent postoperative opioid prescription fulfillment. †Variables included in the model are outlined in table 1.

Ontario, Canada, the receipt of a peripheral nerve block did not appear to be associated with a reduction in persistent postoperative opioid prescription fulfillment. Although our primary analysis demonstrated a statistically significant association (adjusted odds ratio = 0.90; 95% CI, 0.83 to 0.97; $P = 0.007$), the clinical significance of this association is unknown given the retrospective nature of this study. In addition, sensitivity and secondary analyses did not support a consistent relationship between nerve blocks and lower rate of postoperative opioid prescription fulfillment.

Although a recent consensus statement recommends regional anesthesia techniques be used to reduce opioid consumption after surgery,[35] available evidence is sparse and conflicting. A Cochrane review demonstrated that the use of regional anesthesia can result in reduced chronic pain in thoracotomy and breast cancer surgery,[36] although the methodologic quality of this evidence is intermediate as conclusions were based on a few small randomized controlled studies.[32,37] Mueller *et al.*[15] conducted a retrospective study on patients undergoing total shoulder arthroplasty and found no association in the risk of persistent opioid use between postoperative days 91 and 365 (adjusted odds ratio = 0.997; 97.5% CI, 0.875 to 1.14; $P = 0.95$). They also found that the association was not modified with preoperative opioid use. Although our study is also retrospective, it differs from that of Mueller *et al.* in a number of ways. First, Mueller *et al.* utilized billing codes that were not validated for their definition of the peripheral nerve block, whereas we utilized a validated peripheral nerve block exposure code for our study. Second, their population was restricted to patients with private insurance who were less than 65 yr old. In contrast, we were able to evaluate the association of peripheral nerve blocks with persistent postoperative opioid prescription fulfillment across all adult patients in a universal health care system over 6 yr using contemporary data.

We also examined the association of peripheral nerve blocks and persistent postoperative opioid prescription fulfillment by preoperative opioid use status (*e.g.*, opioid-naive, -exposed, or -tolerant) as defined *a priori* in our protocol. In opioid-exposed patients (n = 10,547), the receipt of a peripheral nerve block was associated with reduced odds of persistent postoperative opioid prescription fulfillment in our primary analysis (adjusted odds ratio = 0.86; 95% CI, 0.77 to 0.96; $P = 0.006$), but this association did not persist in the coarsened exact matching sensitivity analysis (which estimates the average treatment effect in the treated, reflecting that the matched group that received peripheral nerve blocks ended up with an increase in opioid fulfillment, similar to those patients without blocks). In addition, we did not find a difference in the number or quantity of immediate postoperative opioid prescriptions between exposure groups in the 14 days after surgery, which demonstrates that the receipt of a peripheral nerve block did not modify the amount of opioids available for patients in the immediate postoperative period. Therefore, we cannot conclude that

Table 4. Sensitivity Analyses Using Multivariable Regression Models

Cohort	Exposure Subgroup	Persistent Postoperative Opioid* n (%)	Adjusted Odds Ratio (95% CI)†	*P* Value
Full (n = 48,523)	Peripheral nerve block type			
	No peripheral nerve block (n = 18,146)	3,221 (17.8)	Reference	
	Peripheral nerve block (single shot; n = 29,008)	4,784 (16.5)	0.90 (0.83–0.97)	0.007
	Peripheral nerve block (catheter; n = 1,369)	224 (16.3)	1.00 (0.86–1.17)	0.974
Opioid-naive (n = 36,865)	Peripheral nerve block type			
	No peripheral nerve block (n = 13,541)	1,054 (7.8)	Reference	
	Peripheral nerve block (single shot; n = 22,224)	1,700 (7.6)	0.94 (0.85–1.03)	0.173
	Peripheral nerve block (catheter; n = 1,100)	108 (9.8)	1.26 (0.96–1.67)	0.098
Opioid-exposed (n = 10,547)	Peripheral nerve block type			
	No peripheral nerve block (n = 4,142)	1,890 (45.6)	Reference	
	Peripheral nerve block (single shot; n = 6,165)	2,697 (43.7)	0.86 (0.77–0.96)	0.008
	Peripheral nerve block (catheter; n = 240)	103 (42.9)	0.82 (0.61–1.10)	0.188
Opioid-tolerant (n = 1,111)	Peripheral nerve block type			
	No peripheral nerve block (n = 463)	277 (59.8)	Reference	
	Peripheral nerve block (single shot; n = 619)	387 (62.5)	0.82 (0.81–1.42)	0.618
	Peripheral nerve block (catheter; n = 29)	13 (44.8)	0.46 (0.262–0.79)	0.005
Full (n = 48,523)	Anesthetic type			
	General anesthesia (n = 17,790)	3,150 (17.7)	Reference	
	Peripheral nerve block/general anesthesia (n = 26,582)	4,409 (16.6)	0.90 (0.84–0.98)	0.012
	Peripheral nerve block with sedation (n = 3,795)	599 (15.8)	0.97 (0.83–1.14)	0.719
	Sedation with local (n = 356)	71 (19.9)	1.34 (0.98–1.80)	0.071
Full (n = 48,523)	Surgery type			
	Total/partial arthroplasty (n = 334)	83 (24.9)	Reference	0.156
	Arthroscopic shoulder procedure (n = 10,259)	1,984 (19.3)	1.42 (0.87–2.31)	
	Open shoulder procedure (n = 37,527)	6,101 (16.3)	1.33 (0.84–2.09)	0.224
	Other procedure (n = 403)	61 (15.1)	1.22 (0.66–2.28)	0.525

$P < 0.05$ is statistically significant.

*Consensus definition of persistent postoperative opioid. †Variables included in the adjusted model include all variables which were included in the primary analysis model (table 2).

opioid-exposed patients benefit to a greater extent than opioid-naive patients with the placement of a peripheral nerve block.

In our *post hoc* analysis, we examined a second commonly used definition for persistent postoperative opioid prescription fulfillment (patients with more than 1 opioid prescription within 1 to 90 days after surgery and [a] more than 10 opioid prescriptions or [b] a 120-day supply of opioids within 91 to 365 days after surgery). Using this definition with a more restrictive criterion than the consensus definition in the primary analysis, there was a statistically significant association between peripheral nerve block receipt with reduced opioid prescription fulfillment. Again, there was lack of consistency of these results within the matched cohort, so these *post hoc* results require cautious interpretation.

Prespecified sensitivity analyses suggest that the use of a catheter techniques in the full population (n = 48,523) were not associated with a decrease in persistent opioid prescription fulfillment. In a small number of opioid-tolerant individuals (n = 1,111), the use of a catheter in 29 patients was associated with reduced odds of persistent postoperative opioid prescription fulfillment (adjusted odds ratio = 0.46; 95% CI, 0.26 to 0.79). Given the small sample size and exploratory nature of this finding, further study is required to examine the potential long-term benefit for catheter-based peripheral nerve block techniques. Although we found that patients who received a peripheral nerve block may require fewer oral morphine equivalents in the year after surgery than those who did not, this finding was not robust to different modeling assumptions. Last, in our model, it appeared that the year of surgery may have modified persistent postoperative opioid prescription fulfillment, with less persistent postoperative opioid use seen in more recent years. This is an encouraging finding, as it is consistent with current public health messaging in an attempt to reduce opioids for the management of chronic pain.[38]

Limitations

Given that this is a retrospective cohort study using administrative data, our findings are at risk of different forms of bias. Specifically, misclassification and confounding bias are key considerations when using administrative data. We used validated measures of exposure to attempt to decrease the risk of misclassification. Our outcome was defined using a consensus best practice definition applied to pharmacy data, which suggests a low likelihood of outcome misclassification.[6] We additionally demonstrated

consistency over two different definitions of postoperative opioid prescription fulfillment in our *post hoc* analysis. Even so, as opioid prescription fulfillment was used as our outcome, it is possible that the opioid prescription fulfillment may be over- or underestimated if a portion of the prescription time frame fell outside our time frame definition. Furthermore, reflecting the pragmatic intentions of our data and design, we are only able to examine whether a peripheral nerve block was provided, but cannot evaluate whether it worked, what technique was used, or which medications were administered at the time of surgery. Similarly, our data provide quantities of opioids dispensed, but not whether they were consumed. In addition, we do not have data specific to reported pain outcomes between the different exposure groups, so we cannot comment on the impact of peripheral nerve blocks on important patient outcomes (*e.g.*, pain-specific outcomes and side effects, opioid side effects). Regarding the effect modification of opioid exposure subgroups, our model may have been underpowered to detect a statistically significant effect in our model. Confounding and indication bias were also possible, although the baseline balance between groups was reassuring, robust adjustment was made for measurable covariates, and primary findings were consistent across different approaches to analysis. As this study was conducted in the province of Ontario, the findings may not generalize to other jurisdictions. In addition, our study was limited to ambulatory procedures, so it may not be generalizable to inpatient shoulder surgeries.

Conclusions

Perioperative interventions that decrease chronic postoperative opioid use are needed. Shoulder surgery is a common, painful procedure for which opioids are routinely dispensed. This retrospective observational study suggests that peripheral nerve blocks do not contribute to reducing persistent postoperative opioid prescription fulfillment in patients undergoing ambulatory shoulder surgery.

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Competing Interests

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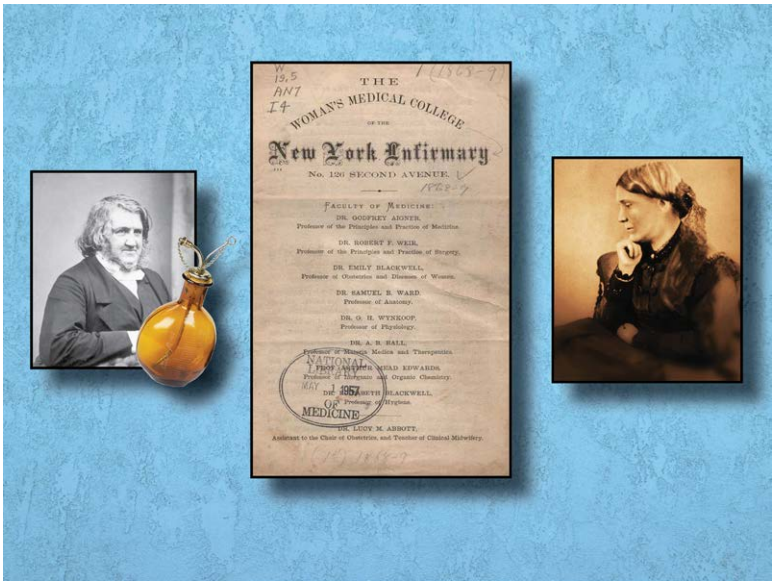
Skirting Male Chauvinism in Physician Training: Dr. Emily Blackwell and the Woman's Medical College



After overcoming great obstacles, Emily Blackwell, M.D. (1826 to 1910), the brilliant and bold younger sister of Elizabeth Blackwell, M.D., became the third woman to earn her medical degree in the United States. A month after her graduation in 1854, she boarded a transatlantic steamship to seek a training opportunity with Professor James Y. Simpson, renowned pioneer of chloroform anesthesia and Chair of Midwifery at the University of Edinburgh. To Emily's relief, Simpson welcomed her warmly and offered to help her achieve her goals. She marveled at his diagnostic acumen and skill with chloroform administration. However, Emily soon found herself *seeing* more than *doing*. Writing to sister Elizabeth, Emily voiced the hunger of countless women physicians who would follow: "The difficulties are by no means great if the places of study were open. Give me the opportunities [Simpson's] assistant has had. I would be more skillful than he is." The sisters Blackwell dreamed of a world in which women could reach their full professional potential. To that end, they founded their own Woman's Medical College of the New York Infirmary (est. 1868), which provided rigorous clinical training and "held open the door for women until broader gates…sw[a]ng wide for their admission." Once medical schools in the United States became coeducational, the Woman's Medical College would close. (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology.)

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