Variations in the Use of Perioperative Multimodal Analgesic Therapy

Karim S. Ladha, M.D., M.Sc., Elisabetta Patorno, M.D., Dr.P.H., Krista F. Huybrechts, M.S., Ph.D., Jun Liu, M.D., M.S., James P. Rathmell, M.D., Brian T. Bateman, M.D., M.Sc.

ABSTRACT

Background: Practice guidelines for perioperative pain management recommend that multimodal analgesic therapy should be used for all postsurgical patients. However, the proportion of patients who actually receive this evidence-based approach is unknown. The objective of this study was to describe hospital-level patterns in the utilization of perioperative multimodal analgesia.

Methods: Data for the study were obtained from the Premier Research Database. Patients undergoing below-knee amputation, open lobectomy, total knee arthroplasty, and open colectomy between 2007 and 2014 were included in the analysis. Patients were considered to have multimodal therapy if they received one or more nonopioid analgesic therapies. Mixed-effects logistic regression models were used to estimate the hospital-specific frequency of multimodal therapy use while adjusting for the case mix of patients and hospital characteristics and accounting for random variation.

Results: The cohort consisted of 799,449 patients who underwent a procedure at 1 of 315 hospitals. The mean probability of receiving multimodal therapy was 90.4%, with 95% of the hospitals having a predicted probability between 42.6 and 99.2%. A secondary analysis examined whether patients received two or more nonopioid analgesics, which gave an average predicted probability of 54.2%, with 95% of the hospitals having a predicted probability between 9.3 and 93.2%.

Conclusions: In this large nationwide sample of surgical admissions in the United States, the authors observed tremendous variation in the utilization of multimodal therapy not accounted for by patient or hospital characteristics. Efforts should be made to identify why there are variations in the use of multimodal analgesic therapy and to promote its adoption in appropriate patients. **(Anesthesiology 2016; 124:837-45)**

POSTOPERATIVE pain is a significant issue for the millions of patients undergoing surgery in the United States each year. Effective treatment of postsurgical pain has been shown to decrease the incidence of chronic pain, improve patient satisfaction, and decrease resource utilization.[1–4] Yet despite efforts to improve the provision of perioperative analgesia, the proportion of patients reporting moderate to severe pain after surgery has remained constant over the past decade.[5,6]

Although opioids provide effective analgesia, their use can be limited by side effects in the perioperative period.[7] Multimodal analgesia refers to the use of two or more drugs or nonpharmacologic interventions with differing mechanisms. Its use has been demonstrated to limit the amount of opioids consumed and provide more effective pain control than opioids alone.[8–10] Component therapies of multimodal analgesia with substantial evidence to support efficacy in postoperative patients include gabapentinoids,[11–13] acetaminophen,[14,15] ketamine,[16,17] nonsteroidal antiinflammatory drugs (NSAIDs),[18,19] and regional anesthesia.[20,21]

What We Already Know about This Topic

- Using complementary pharmacologic and nonpharmacologic interventions for pain relief (multimodal analgesia) in the postoperative period has been recommend for several years
- Whether multimodal analgesia is commonly practiced across hospitals is not known

What This Article Tells Us That Is New

- In a review of nearly 800,000 patients undergoing four common major surgical procedures between 2007 and 2014, the probability of receiving multimodal analgesia was high (90%)
- There was large variability among hospitals in the use of multimodal analgesia, which could not be accounted for by patient or hospital characteristics

The sum of the currently available evidence, even after the exclusion of numerous studies in this field that were found to be fraudulent, suggests that the routine use of multimodal analgesia should be the standard of care.[8,22] Indeed, current practice guidelines for perioperative pain management recommend that multimodal therapy be used in all postsurgical

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patients.[23] However, the proportion of patients who actually receive this evidence-based approach is unknown. The objective of this study was to describe hospital-level patterns in the utilization of perioperative multimodal analgesia for four common noncardiac surgeries: open colectomy, total knee arthroplasty, open lobectomy, and below-knee amputation. These operations were selected to represent major intraabdominal, orthopedic, noncardiac thoracic, and vascular surgical procedures respectively. We hypothesized that there would be substantial variation in the use of multimodal therapy not explained by patient or hospital characteristics.

Materials and Methods

Data Source

Data for the study were obtained from the Premier Research Database and included patients undergoing a surgical procedure from the fourth quarter of 2007 until the third quarter of 2014. Premier is a hospital-based database that includes *International Classification of Diseases*, 9th Revision, *Clinical Modification* discharge diagnoses codes. The database also contains detailed information on all charges for procedures performed and medications administered during an inpatient hospitalization. The database has been previously used to evaluate the safety and patterns of use of inpatient medications.[24–30] The use of these deidentified data for research was approved by the Partners Institutional Review Board (Boston, Massachusetts).

Cohort

By using ICD-9 codes, we identified adult patients undergoing four types of surgical procedures: below-knee amputation, open lobectomy, total knee arthroplasty, and open colectomy. The use of ICD-9 codes to differentiate between open and minimally invasive lobectomies and colectomies has been well established in the previous literature.[31–35] In addition, we excluded patients with any codes or charges that suggested a laparoscopic or video-assisted thoracoscopic surgery because the smaller incisions might alter the approach to pain management. We also excluded patients younger than 18 yr because pediatric pain management is a separate entity. We restricted our analysis to hospitals with greater than 10 procedures for each surgery type in the database because smaller numbers of procedures would yield unstable estimates of multimodal therapy use. The final cohort included 315 hospitals.

Exposure

Exposure was defined on the basis of charges generated at any time from the day of surgery until the day of discharge. We identified patients who received regional blockade with local anesthetics, *i.e.*, epidural placement and peripheral nerve blocks, oral cyclooxygenase-2 selective NSAIDs, nonselective NSAIDs, calcium channel α-2-δ antagonists (gabapentinoids), ketamine, and acetaminophen. The full list of medications included in these categories can be found in Supplemental Digital Content 1, http://links.lww.com/ALN/B248, and the complete set of codes can be obtained on request from the corresponding author. Patients were considered to have multimodal therapy if they received one or more of these nonopioid analgesic therapies. In a secondary analysis, we examined the proportion of patients who received two or more nonopioid therapies.

Covariates

We considered five groups of covariates, which could relate to multimodal analgesia use. These included (1) surgery type; (2) patient demographics and year of procedure; (3) medical comorbidities; (4) pain-related conditions, psychiatric comorbidities, and psychoactive medication use; and (5) hospital characteristics. We assessed the following patient demographics: gender, age, and race/ethnicity. Medical comorbidities were defined based on the presence of diagnosis codes during the surgical hospitalization.[36] These included renal disease, ischemic heart disease, congestive heart failure, cerebrovascular disease, chronic pulmonary disease, diabetes, coagulopathy, liver disease, acquired immunodeficiency syndrome/human immunodeficiency virus, paralysis, peptic ulcer disease, valvular disease, pulmonary circulation disorders, seizure disorders, and other neurologic disorders. Pain conditions and psychiatric comorbidities were assessed in a similar manner and included malignancy, back pain, fibromyalgia, chronic pain, rheumatoid arthritis, migraines, anxiety, depression, dementia, personality disorder, and psychoses. Psychoactive medication usage during the surgical hospitalization was also assessed and included the use of anxiolytics, antidepressants, antipsychotics, and anticonvulsants (excluding gabapentinoids). We also considered the following hospital characteristics: urban (*vs.* rural) location, geographic region (categorized as Midwest, Northeast, South, and West), teaching status, and annual procedure volume tertile (based on the total procedure volume during the study time period, categorized as low [66 to 302], medium [303 to 509], or high [511 to 1838]). A full list of covariates and associated codes can be found in Supplemental Digital Content 1, http://links.lww.com/ALN/B248.

Statistical Analysis

The proportion of patients who received multimodal therapy was determined for each hospital, and hospitals were divided into quartiles based on the overall proportion of patients who received multimodal therapy. Patient and hospital characteristics that were likely to influence the use of multimodal therapy were stratified by hospital quartile and compared with a chi-square test.

We used mixed-effects logistic regression models to estimate the hospital-specific frequency of multimodal therapy while adjusting for patient case mix and hospital characteristics as well as to account for random variation.

Table 1. Usage of Analgesic Technique Across Surgical Procedures

	Total	Any Nonopioid Analgesic	More than One Nonopioid Analgesic	Regional Anesthesia	Acetaminophen	Cyclooxygenase-2 Inhibitors	Nonspecific Nonsteroidal Antiinflammatory Drugs	Gabapentinoids	Ketamine	Any Opioid
Below-knee amputation	32,375	25,920 (80.1)	11,758 (36.3)	855 (2.6)	21,329 (65.9)	420 (1.3)	4,727 (14.6)	11,562 (35.7)	1,664 (5.1)	31,217 (96.4)
Colectomy	171,942	122,533 (71.3)	44,056 (25.6)	10,083 (5.9)	96,060 (55.9)	1,579 (0.9)	53,769 (31.3)	7,348 (4.3)	4,121 (2.4)	166,241 (96.7)
Lobectomy	23,696	20,643 (87.1)	12,870 (54.3)	6,326 (26.7)	15,070 (63.6)	494 (2.1)	13,454 (56.8)	1,909 (8.1)	628 (2.7)	22,834 (96.4)
Total knee arthroplasty	571,436	516,770 (90.4)	376,208 (65.8)	81,871 (14.3)	398,881 (69.8)	220,191 (38.5)	285,667 (50.0)	126,178 (22.1)	23,402 (4.1)	555,209 (97.2)

Values are represented as n (%).

For each model, a variable identifying each hospital was added as a random intercept, and patient- and hospital-level covariates were incorporated as fixed effects. The hospital-specific intercept represents the hospital-specific frequency for multimodal therapy use after adjusting for covariates.[37,38]

We used sequential mixed-effects models with increasing levels of adjustment to assess the relative influence of different patient and hospital characteristics for between-hospital variation in multimodal therapy use. After adjusting for all patient and hospital level characteristics, the hospital-specific intercepts represented the hospital-level tendency to utilize multimodal therapy independent of covariates.

Due to the large number of covariates, we used propensity scores as a data reduction technique.[37,38] For each stage of sequential adjustment, a separate propensity score was estimated to predict exposure to multimodal therapy and included in the mixed-effects model. The propensity score was centered on the mean so that the random intercept for an individual hospital represented the probability that an average patient would be treated with multimodal therapy in a given hospital.

We performed two additional analyses to better interpret the trends discovered in the primary analysis. First, we repeated the analysis but varied the definition of the exposure based on the two time periods: the day of surgery and the days after surgery until discharge. This was undertaken to investigate the dynamics of the perioperative period. Specifically, because anesthesiologists decide which analgesics are administered on the day of surgery, this variation may be less compared with that found on subsequent days. In addition, we repeated the primary analysis in subgroups defined by surgical procedure. This was performed to ensure that the results of the primary analysis were not driven by the most common surgery, *i.e.*, total knee arthroplasty and to determine whether the use of multimodal therapy varied by procedure. As with the primary analysis, the propensity score was reestimated for each model in the sub-group analyses. All analyses were performed in SAS (version 9.3; SAS, USA), and mixed-effects model were run using the NLMIXED command.

Results

The cohort included 799,449 patients who underwent a procedure at any of the 315 hospitals of which 4% underwent a below-knee amputation, 22% underwent a colectomy, 3% underwent a lobectomy, and 71% underwent a total knee arthroplasty. Of all the patients, 97% received an opioid, whereas 66% received acetaminophen. The usage of individual analgesics varied by surgery type. For example, the rate of regional anesthesia was 27% among patients undergoing lobectomy but only 3% for those undergoing below-knee amputation. The usage of each analgesic by surgery type is displayed in table 1. The observed (crude)

overall usage of multimodal therapy was 85.8% among all patients, and the median hospital utilization rate was 89.5% (interquartile range, 80.8 to 94.0%). We stratified hospitals based on the proportion of patients treated with multimodal therapy, and differences between quartiles for each covariate were assessed. The lowest quartile had a greater proportion of low-volume centers and black patients when compared with the highest quartile. Patients in the highest quartile were more likely to be using an antidepressant and have chronic pain but less likely to have a solid tumor compared with the lowest quartile. Covariates and differences across quartiles are fully displayed in table 2 and Supplemental Digital Content 2, http://links.lww.com/ALN/B249.

Table 2. Selection of Patient- and Hospital-level Characteristics According to Quartile of Multimodal Therapy Usage

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	*P* Value
No. of patients	165,966	184,953	209,969	238,561	
No. of hospitals	78	79	80	78	
Percentage of patients receiving multimodal therapy, median (range)	71.3 (0.1–80.7)	85.7 (80.8–89.4)	92.4 (89.5–94.0)	96.0 (94.0–99.0)	
Surgery type					
Below-knee amputation	8,012 (4.8)	8,339 (4.5)	8,633 (4.1)	7,391 (3.1)	< 0.0001
Open colectomy	46,419 (28.0)	43,114 (23.3)	45,554 (21.7)	36,855 (15.5)	
Open lobectomy	5,474 (3.3)	5,756 (3.1)	6,264 (3.0)	6,202 (2.6)	
Total knee replacement	106,061 (63.9)	127,744 (69.1)	149,518 (71.2)	188,113 (78.9)	
Demographics					
Male	67,304 (40.6)	74,491 (40.3)	86,227 (41.1)	96,669 (40.5)	< 0.0001
Age (yr)					
18–30	2,011 (1.2)	1,728 (0.9)	1,934 (0.9)	1,444 (0.6)	< 0.0001
31–40	3,501 (2.1)	3,267 (1.8)	3,489 (1.7)	3,096 (1.3)	
41–50	13,235 (8.0)	12,937 (7.0)	14,218 (6.8)	14,492 (6.07)	
51–60	37,297 (22.5)	40,388 (21.8)	46,807 (22.3)	51,456 (21.6)	
61–70	52,462 (31.6)	61,346 (33.2)	69,448 (33.1)	81,838 (34.3)	
71–80	40,984 (24.7)	47,738 (25.8)	53,628 (25.5)	63,600 (26.7)	
≥ 81	16,476 (9.9)	17,549 (9.5)	20,445 (9.7)	22,635 (9.5)	
Race					
Other	34,798 (21.0)	37,584 (20.3)	27,800 (13.2)	40,205 (16.9)	< 0.0001
Black	20,196 (12.2)	20,437 (11.1)	16,393 (7.8)	15,243 (6.4)	
White	110,972 (66.9)	126,932 (68.6)	165,776 (79.0)	183,113 (76.8)	
Hospital characteristics					
Teaching hospital	72,542 (43.7)	93,153 (50.4)	93,961 (44.8)	90,678 (38.0)	< 0.0001
Procedure volume					
Low	44,075 (26.6)	35,170 (19.0)	26,507 (12.6)	18,206 (7.6)	< 0.0001
Middle	51,788 (31.2)	51,971 (28.1)	68,675 (32.7)	57,765 (24.2)	
High	70,103 (42.2)	97,812 (52.9)	114,787 (54.7)	162,590 (68.2)	
Pain-related conditions and psychiatric comorbidities					
Alcohol abuse	2,905 (1.8)	3,274 (1.8)	3,700 (1.8)	3,632 (1.5)	< 0.0001
Drug abuse	2,328 (1.4)	2,677 (1.5)	2,777 (1.3)	2,637 (1.1)	< 0.0001
Tobacco abuse	35,354 (21.3)	46,567 (25.2)	50,080 (23.9)	59,342 (24.9)	< 0.0001
Back pain	9,455 (5.7)	11,030 (6.0)	13,315 (6.3)	17,801 (7.5)	< 0.0001
Chronic pain	4,646 (2.8)	5,929 (3.2)	6,283 (3.0)	9,992 (4.2)	< 0.0001
Metastatic cancer	8,433 (5.1)	7,488 (4.1)	7,845 (3.7)	7,079 (3.0)	< 0.0001
Solid tumor	21,510 (13.0)	20,858 (11.3)	21,316 (10.2)	19,051 (8.0)	< 0.0001
Anxiety	12,267 (7.4)	14,683 (7.9)	13,924 (6.6)	17,678 (7.4)	< 0.0001
Depression	21,040 (12.68)	26,053 (14.09)	27,882 (13.28)	33,696 (14.12)	< 0.0001
Medication usage					
Anxiolytic	40,863 (24.62)	49,329 (26.67)	55,316 (26.34)	60,894 (25.53)	< 0.0001
Antidepressant	31,206 (18.80)	42,799 (23.14)	51,586 (24.57)	57,982 (24.30)	< 0.0001
Medical comorbidities					
Chronic pulmonary disease	31,763 (19.14)	35,459 (19.17)	37,586 (17.90)	40,907 (17.15)	< 0.0001
Diabetes	40,972 (24.69)	46,684 (25.24)	49,883 (23.76)	53,607 (22.47)	< 0.0001
Ischemic heart disease	8,040 (4.84)	9,585 (5.18)	10,167 (4.84)	10,350 (4.34)	< 0.0001
Renal disease	14,000 (8.44)	15,459 (8.36)	15,402 (7.34)	16,196 (6.79)	< 0.0001

Additional covariates incorporated into the mixed-effects models are listed in Supplemental Digital Content 2, http://links.lww.com/ALN/B249.

The results of the sequential mixed-effects logistic regression models with demographics, medical comorbidities, pain-related conditions and psychiatric comorbidities, and hospital-level covariates added at each step are shown in table 3. The between-hospital variance in the use of multimodal therapy is described by σ_b^2. If the between-hospital variation in multimodal therapy use is fully explained by the covariates, σ_b^2 would be expected to approach 0, and all hospitals would be predicted to have the same probability of multimodal therapy use. In the unadjusted model, the σ_b^2 (SE) was 1.75 (0.14), and when controlling for all covariates, the σ_b^2 decreased slightly to 1.68 (0.14). Thus, the variation observed was not explained by patient- or hospital-level factors. The unadjusted mixed-effects model generated a mean predicted probability of exposure to multimodal of 87.9% and 95% of the hospitals had a predicted probability between 35.2 and 99.0%. These estimates remove random variation compared with the crude estimates but do not account for potential between-hospital differences in patient and hospital characteristics. In the fully adjusted model (accounting for patient and hospital characteristics), the mean predicted probability was 90.4%, with 95% of the hospitals having a predicted probability between 42.6 and 99.2%.

The predicted probabilities of multimodal therapy use for each hospital in rank order in the unadjusted and fully adjusted models are presented in figure 1A. We observed little attenuation of the variation in use of multimodal therapy when accounting for a broad range of patient and hospital characteristics.

In a secondary analysis, we examined whether patients received two or more nonopioid analgesics, which may confer additional benefits to the patient by targeting additional pain pathways. Within the entire cohort, the observed proportion of patients who received more than one nonopioid analgesic was 55.7%, and the median hospital utilization was 54.6% (interquartile range, 37.5 to 68.2%). In the unadjusted model, the σ_b^2 (SE) was 1.54 (0.13), and after adjustment for all covariates, the σ_b^2 increased to 1.56 (0.13), again suggesting that the variation is not explained by the patient and the hospital factors included in the model. In the unadjusted mixed-effects model, the predicted mean probability of receiving two or more nonopioid analgesics was 51.1% (95% range of 8.4 to 92.3). In the fully adjusted model, the average predicted probability was 54.2%, with 95% of the hospitals having a predicted probability between 9.3 and 93.2%. The results from the sequential models in the secondary analysis are presented in Supplemental Digital Content 3, http://links.lww.com/ALN/B250. The predicted probabilities of receiving two or more nonopioid analgesics for each hospital in rank order in the unadjusted and fully adjusted models are presented in figure 1B. Similar to the initial exposure definition, there was little change in the variation observed when controlling for covariates.

When the exposure definition was divided into two time periods (day of surgery and days after surgery), a greater proportion of patients received a nonopioid analgesic on the days after surgery compared with the day of surgery (80 *vs.* 65%). The same trend, although less pronounced, occurred when examining the use of two or more nonopioid analgesics (38 *vs.* 34%). The complete list of proportions for each individual analgesic separated by perioperative time period can be found in Supplemental Digital Content 4, table S5, http://links.lww.com/ALN/B251. When using mixed-effects models, there was little change in the variation between the unadjusted and fully adjusted models (Supplemental Digital Content 4, tables S6 and S7, http://links.lww.com/ALN/B251). Figure 2

Table 3. Estimated Hospital-level Usage Rate of One or More Nonopioid Analgesics Based on Mixed-effects Models with Increasing Levels of Adjustment for Patient- and Hospital-level Factors

			Multimodal Therapy Usage Rate (%)		
Models	β_0 (SE)*	σ^2 (SE)†	Average Hospital‡	2.5 Percentile§	97.5 Percentile
Unadjusted	1.98 (0.075)	1.75 (0.14)	87.87	35.20	98.97
Adjusted for					
Surgery type	2.18 (0.076)	1.80 (0.15)	89.92	39.04	99.20
Surgery type, *demographics, year of hospitalization*	2.18 (0.076)	1.80 (0.15)	89.86	38.91	99.19
Surgery type, demographics, year of hospitalization, *medical comorbidities*	2.18 (0.076)	1.80 (0.15)	89.84	38.88	99.19
Surgery type, demographics, year of hospitalization, medical comorbidities, *pain-related conditions, psychiatric comorbidities, medication usage*	2.18 (0.075)	1.74 (0.14)	89.83	39.91	99.16
Surgery type, demographics, year of hospitalization, medical comorbidities, pain-related conditions, psychiatric comorbidities, medication usage, and *hospital characteristics*	2.24 (0.073)	1.68 (0.14)	90.43	42.64	99.18

*β_0 is the marginal (averaged across hospitals) odds of using multimodal therapy for a patient with the mean propensity score. †Estimate of the between-hospital variation. The random intercept b_j for each hospital is assumed to be normally distributed with mean 0 and variance σ^2. σ^2 represents the hospital-specific deviation from β_0. With the increasing levels of adjustment, there is a less unexplained variation and σ_b^2 is expected to decrease. ‡Prescribing proportion for the "average" patient, defined as a patient with a mean propensity score. The average differs slightly between models because different factors are being adjusted for in the various models; it is estimated as $\exp(\beta_0)/[1 + \exp(\beta_0)]$. §Range determined from observed predicted values.

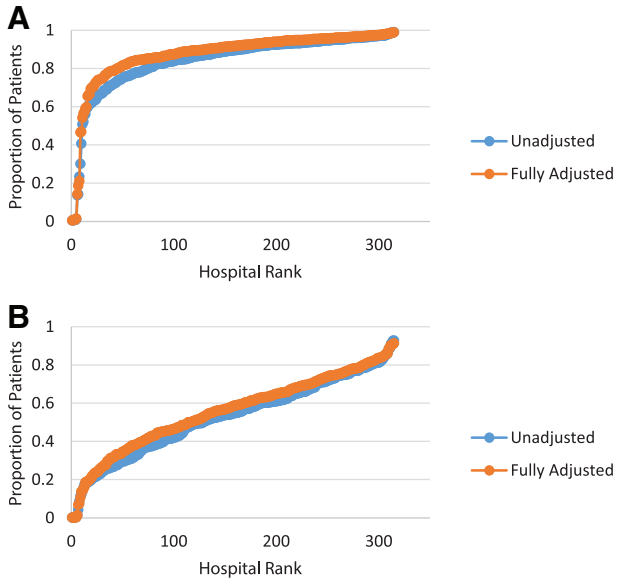

Fig. 1. Range of predicted proportions of the use of multimodal therapy obtained from unadjusted and fully adjusted mixed-effects models in the entire cohort. (*A*) The rate of use of one or more nonopioid analgesics. (*B*) The estimated proportion of patients receiving two or more nonopioid analgesics at each hospital.

displays the range of predicted proportions across hospitals for both time periods.

The mixed-effects models were also run for each individual surgery type. The range of multimodal therapy usage did vary by surgical procedure. When examining the use of more than one nonopioid analgesic, the mean predicted probability of exposure to multimodal therapy in the fully adjusted model was 84.4% (95% range, 40.6 to 97.7%) for patients undergoing below-knee amputations compared with 73.1% (95% range, 32.4 to 93.9%) for patients who had a colectomy. Similar to the primary analysis, there was little change in the variation between the fully adjusted and unadjusted models. The complete results from the models for each surgery type can be found in Supplemental Digital Content 5, http://links.lww.com/ALN/B252. Figure 3 displays the ranges of multimodal use for each surgical procedure from the fully adjusted mixed-effects models. Of note, when examining the use of one or more nonopioid analgesics in patients undergoing total knee arthroplasty, the fully adjusted model did not converge and estimates could not be obtained.

Discussion

In this large, nationwide sample of surgical admissions in the United States, we observed tremendous variation in the use of multimodal therapy. Adjustment for patient demographics, comorbidities, and hospital characteristics did not mitigate this variation because the majority of hospitals had a utilization rate ranging from 43 to 99% in the fully adjusted model. When extending the analysis to the use of two or more nonopioid analgesics, the range was even wider with 95% of the hospitals ranging from 8 to 92%. This analysis suggests that the use of

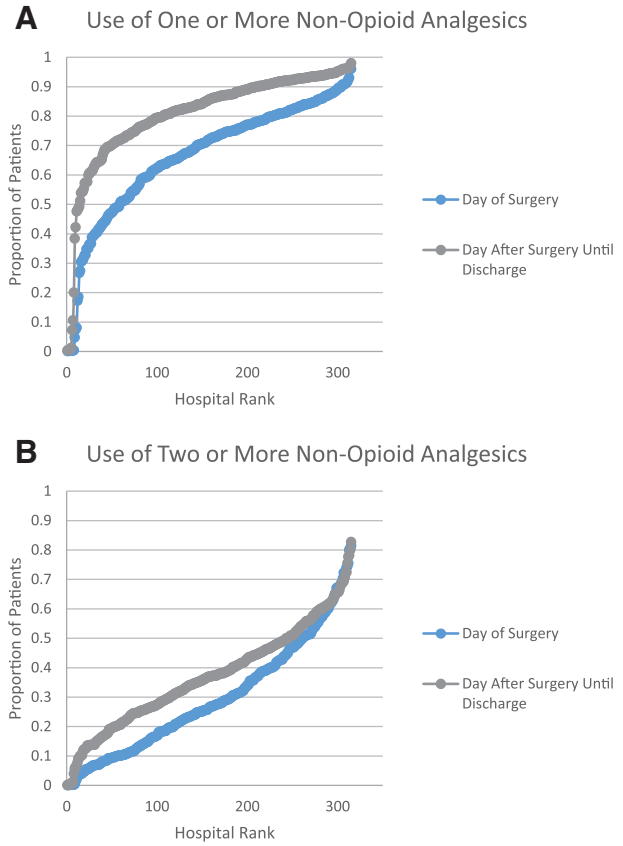

Fig. 2. Range of predicted proportions of the use of multimodal therapy obtained from fully adjusted mixed-effects models grouped by perioperative time period. (*A*) The rate of use of one or more nonopioid analgesics. (*B*) The estimated proportion of patients receiving two or more nonopioid analgesics at each hospital.

multimodal therapy is based on nonmedical and institution-specific factors such as local hospital culture and individual physician preference independent of patient or hospital characteristics. We also found that the usage of multimodal therapy varied by surgical procedure, and multimodal analgesia was less prevalent on the day of surgery compared with the days after surgery.

This analysis represents, to the best of our knowledge, the first empiric description of the use of multimodal therapy in the United States. The use of multimodal therapy has been recommended by numerous societies as a strategy that should be implemented whenever possible.[23,39,40] The results of our analysis demonstrate that these recommendations have not been universally adopted. In our cohort, nearly all patients received an opioid; however, they did not consistently receive an additional nonopioid analgesic. The incidence of side effects due to opioids is high in the perioperative period with gastrointestinal- and central nervous system–related adverse event rates ranging as high as 30%.[41] These adverse reactions have been implicated in significant increases in mortality, cost, lengths of stay, and readmission rates.[7,42,43] Several previous studies have demonstrated that combinations of analgesic agents lead to more effective pain control with fewer side effects.[8–10] Therefore, expanding the

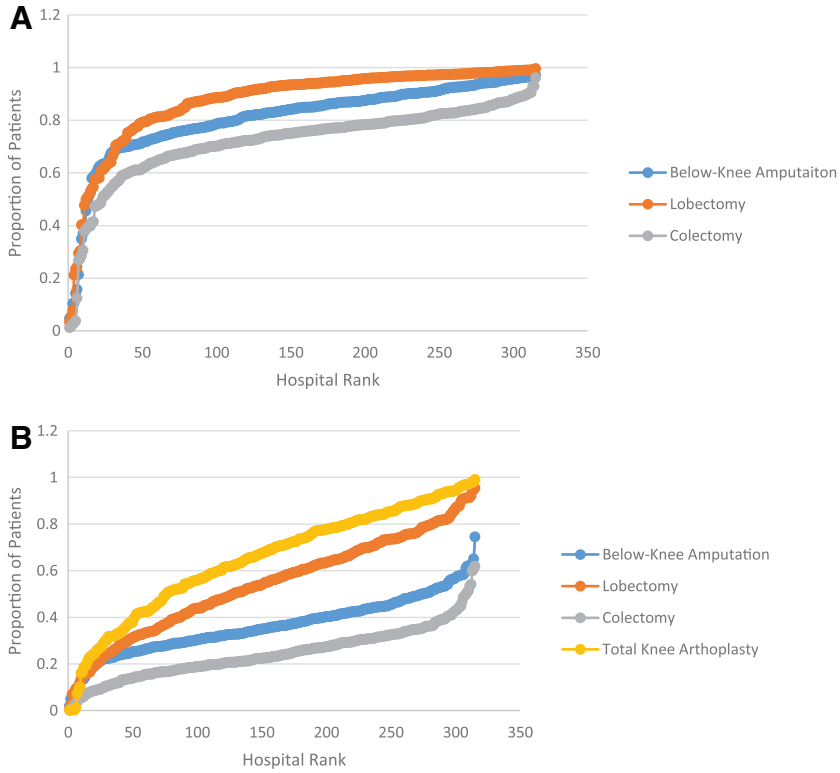

Fig. 3. Range of predicted proportions of the use of multimodal therapy obtained from fully adjusted mixed-effects models grouped by type of surgery. (*A*) The rate of use of one or more nonopioid analgesics. (*B*) The estimated proportion of patients receiving two or more nonopioid analgesics at each hospital. Of note, the model examining the use of one or more nonopioid analgesics in total knee arthroplasty did not converge, and thus, estimates could not be calculated.

use of nonopioid analgesics can potentially result in improved outcomes and patient satisfaction. Further research should be undertaken to better understand the barriers to administering these medications to all eligible patients.

It is important to note that the variation in practice was greater when examining the use of two or more nonopioid analgesics. Thus, the real opportunity in decreasing variability may be in expanding the use of multiple types of medications, rather than just a single non-opioid analgesic. However, additional study is required to determine the optimal combinations of medications that maximize synergy of analgesia, while minimizing side effects from polypharmacy.

This study has certain limitations inherent to its design. We were unable to control for outpatient medication use before surgery. Patients who are opioid tolerant might be more prone to receiving multimodal therapy, and certain hospitals may have a higher prevalence of these patients. However, the prevalence of patients with drug abuse or dependence (including opioid abuse/dependence) was similar across each of the hospital quartiles, suggesting that this was not an important determinant of the observed patterns. Further, covariates were based on the ICD-9 codes, and the sensitivity of certain codes is limited for some conditions. However, this is unlikely to explain the tremendous variations in practice between institutions, particularly given that the predicted use did not shift significantly with adjustment for measured covariates.

We examined four surgeries, which were selected because they span across four different surgical specialties and there is an evidence base for the benefits of multimodal analgesia with these procedures.[44] However, even among these procedures, we observed differences in the use of multimodal therapy by surgery type. Thus, the variation across other surgical procedures, in which the evidence to support the use of multimodal analgesia is less robust, would likely be even greater than the amount observed in this study. Medication administration was determined by charge codes under the assumption that a patient actually received a medication if he or she was assigned a billing code for it. In our cohort, 97% of patients had a billing code for an opioid suggesting that the rate of potential misclassification of medication administration was small and unlikely to significantly affect the results. Finally, the unit of analysis in our study was the hospital and not individual providers because we did not have provider-level data. Given the multitude of physicians and other healthcare providers who interact with a patient during the perioperative period, it is difficult to identify any single individual as responsible for providing perioperative analgesia. For this reason, the hospital may be the ideal level for action through interventions such as the creation of an acute pain service[45] or the establishment of protocols.

There is no doubt that postoperative pain management should be tailored to individual patients and specific surgical

procedures. For example, elderly patients with certain comorbidities may not be candidates to receive gabapentin or cyclooxygenase-2 inhibitors. However, the results of our study suggest that nonopioid analgesics are underutilized at many institutions. These medications provide a potential cost-effective strategy to improve outcomes and patient satisfaction with a side-effect profile that is superior to opioids alone. We see little reason why the utilization rate of multimodal therapy should not be dramatically higher across all hospitals. Efforts should be made to identify why there are variations in the use of multimodal analgesic therapy in patients undergoing surgery. This represents an opportunity for both surgeons and anesthesiologists to work together to ensure the delivery of multimodal analgesia to each and every patient.

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Competing Interests

The authors declare no competing interests.

Correspondence

Address correspondence to Dr. Ladha: Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital, 1620 Tremont Street, Suite 3030, Boston, Massachusetts 02120. karim.ladha@post.harvard.edu.

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