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POSTOPERATIVE KETOROLAC IN BREAST AND BODY CONTOURING PROCEDURES: A NATIONWIDE CLAIMS ANALYSIS

Brian P. Kelley, MD^a, Kevin C. Chung, MD, MS^b, Ting-Ting Chung, MS^a, Katelyn G. Bennett, MD^a, Gina Sacks, MD^a, Erika D. Sears, MD, MS^{a,c}, and Jennifer F. Waljee, MD, MS^a

^aSection of Plastic Surgery, University of Michigan, Michigan Medicine, 1500 E Medical Ctr Blvd., Ann Arbor, MI 48109

^bProfessor of Surgery, Section of Plastic Surgery, Assistant Dean for Faculty Affairs, University of Michigan Medical School, 1500 E Medical Center Blvd., Ann Arbor, MI 48109

^cVeterans Affairs Center for Clinical Management Research, Ann Arbor, Michigan

Abstract

Background—NSAIDs are useful alternatives to narcotics for analgesia. However, concerns remain regarding their safety. We evaluated ketorolac use and perioperative complications and hypothesized that there is no association between ketorolac and morbidity following outpatient body contouring procedures.

Methods—We utilized the Truven Marketscan claims database to evaluate patients undergoing breast and body contouring surgery. We selected patients who received ketorolac and minimum enrollment of 90 days postoperatively. We performed a multivariable logistic regression to calculate the risk of morbidity and associated numbers needed to treat or harm, adjusting for clinical and sociodemographic factors.

Results—Among the 106,279 patients enrolled, 4,924 patients (4.6%) received postoperative ketorolac. In multivariable regression analysis, ketorolac was not associated with diagnosis of hematoma (OR 1.20; 95% CI 0.99-1.46; $P>0.05$). There was an increased rate of reoperation within 72 hours (OR 1.22; 95% CI 1.00-1.49; $P<0.05$; NNH 262). Ketorolac was associated with significantly fewer readmissions (OR 0.76; 95% CI 0.62-0.93; $P<0.05$; NNT 87) with a reduction in the rate of pain as a diagnosis for admission (0.6% vs 4.3%; $P=0.021$). Ketorolac was associated with seroma, but this association may not be causal (OR 1.28; 95% CI, 1.05-1.57; $P<0.05$; NNH 247). Ketorolac provided an average cost savings of over \$157 per patient.

Conclusions—Despite a small increase in odds for reoperation, the benefits of ketorolac likely outweigh the small risks after surgery. Absolute differences in reoperation rates were low and

Corresponding author and reprint requests sent to: Brian P. Kelley, MD, Section of Plastic Surgery, The University of Michigan Health System, 1500 E. Medical Center Drive, 2130 Taubman Center, SPC 5340, Ann Arbor, MI 48109-5340, Phone: 734-936-5885, Fax: 734-763-5354, kelleybr@med.umich.edu.

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improved rates of hospital readmission impact better cost utilization. Based on these findings, we advocate postoperative ketorolac once the wound is hemostatic.

Patients cite postoperative pain as a chief concern prior to surgery.¹ In contrast, choices in postoperative pain management are difficult given the lack of effective treatment options beyond opioid analgesics and the growing concern for opiate misuse.¹⁻⁷ Considering the alternatives, nonsteroidal anti-inflammatory drugs (NSAIDs) have many desirable characteristics. NSAIDs are commonly used medications in over-the-counter and prescription forms. However, data regarding their efficacy and safety are unclear. Risks such as bleeding, gastritis, myocardial infarction, and renal failure have prompted caution with NSAID use. On the other hand, prior studies suggested safe peri-operative use of common NSAIDs, such as ketorolac and ibuprofen, in plastic surgery.^{8,9} Reversible, non-selective NSAIDs function by temporarily inhibiting the cyclooxygenase (COX) enzymes. As a result, these medications are effective analgesics and anti-inflammatories. However, platelet aggregation is also temporarily inhibited, which prompts concern for the ability to achieve surgical hemostasis. Additionally, there is little evidence on the effect of NSAIDs other peri-operative complications.

Ketorolac, a potent, non-selective NSAID available most commonly in intravenous forms, has been documented to provide excellent postoperative analgesia for a variety of surgical procedures, but, like other NSAIDs, side effect concerns limit use. A few prior studies on patients undergoing surgery have found that ketorolac is generally safe with regard to bleeding.^{8,10,11} However, these studies are mostly underpowered, retrospective, include non-systemic forms of ketorolac delivery, or are not in pertinent patient populations. For example, a recent meta-analysis of ketorolac restricted to plastic surgery patients has not demonstrated an increased risk for hematoma, but this analysis included a mix of studies with different administration routes, including both topical and systemic.¹¹⁻¹³ Excluding the topical use of ketorolac, the two largest studies included in the pooled data were retrospective chart reviews and the conclusions differed.^{10,14}

The escalation of opioid use in the United States has illuminated the need for safe, non-addictive, non-sedating analgesics. Ketorolac, like other reversible NSAIDs, has the potential to be a useful analgesic if its safety can be confirmed. A small group of prior studies tested the efficacy and safety of ketorolac, but no study has definitively characterized the postoperative risks.^{8,10,11,14-17} However, concurrent with the consensus studies, there is growing comfort that ketorolac is likely safe in most operations in healthy patients. To date, no national or population based studies have been conducted on NSAIDs in the postoperative period. Given the lack of power in prior work and to further elucidate the safety and practice patterns of ketorolac in the United States, we evaluated insurance claims from a national database seeking to evaluate national practice patterns in common body contouring operations, including lipectomy and breast reduction. We chose to focus on body contouring procedures because of the relatively high risk and high sensitivity for hematomas in this patient population.¹⁸ Furthermore, we aimed to evaluate the differences in complication occurrence, need for reoperation, and hospital length of stay for patients who received ketorolac perioperatively. We hypothesized that there would be no difference in morbidity between the groups after surgery.

MATERIALS AND METHODS

Data Source and Study Cohort

This study qualified as exempt by the institutional review board. We used the Truven Marketscan Commercial Claims and Encounters and Medicare Supplement and Coordination of Benefits (Marketscan; Truven Health Analytics, Ann Arbor, Mich.) inpatient and outpatient encounters between January 1, 2009 to December 31, 2014.¹⁹ The Marketscan databases contain a national sample of beneficiaries and dependents from large employers, government, and public organizations. The database includes patient-specific health care encounters, timing of care, health care cost, and health plan details for over 55 million enrollees annually. Each patient in the database has a unique identification number, which allows them to be followed longitudinally through enrollment in the included health plan. Patients included were 18 years or older in age, undergoing an outpatient body contouring operation as identified by Current Procedural Terminology (CPT) codes for body contouring procedures, including lipectomy, liposuction, and breast procedures. Appendix 1 provides a comprehensive list of *International Classification of Diseases, Ninth Revision* (ICD-9) and CPT codes used to identify and extract data (See Appendix 1, Supplemental Digital Content 1, which shows the Study Code Definitions..

A total of 158,849 patients met criteria between Jan 1, 2009 to September 30, 2014. No patients were enrolled after Sept 30, 2014 to capture at least 90 days of postoperative enrollment within the database (Fig. 1). Patients were excluded if there was lack of continuous enrollment during the study period, lack of pharmacologic records, claims for systemic anticoagulation (including heparin, low-molecular weight heparin, coumadin, argatroban, or clopidogrel) within 30 days prior to surgery, any prescription NSAID within 7 days prior to surgery (including aspirin), age < 18 years, or any of the complications of interest in the week prior to surgery. Medication exposure was defined by National Drug Codes (NDCs) for each medication in addition to HCPCS procedure-related 'J' codes for infusion or injections.

Ketorolac Exposure

Patients included in the study cohort were enrolled for a minimum of 1 month prior and 3 months after the index surgery. Patients were selected for exposure to intravenous ketorolac claims within 48 hours after surgery, excluding exposure on readmission to the hospital for complications. Exposure to ketorolac was defined by J-1885 (Injection, ketorolac tromethamine, per 15 mg) and NDCs (See Appendix 2, Supplemental Digital Content 2, which shows the NSAID and Ketorolac Exposure.

Outcome Variables

Patients were followed for 90 days from their index operation for complications, readmission for any reason, readmission for pain, reoperation for any reason, and readmission specific to hematoma washout (Appendix 1, Supplemental Digital Content 1. A sub-analysis of readmissions was performed to analyze the rates of admission for either a primary or secondary diagnosis of pain. The dosage of ketorolac was assessed for a difference in rates of complications comparing low dose IV ketorolac (15mg) to high dose

IV ketorolac (30mg). Complications included hematoma, seroma, infection, acute kidney injury, venous thrombosis, pulmonary embolism, myocardial infarction, and blood transfusion. Other drug exposures were tracked by NDCs, including other NSAIDs (See Appendix 3, Supplemental Digital Content 3, which shows the other NSAID Exposure, and systemic anticoagulants (See Appendix 4, Supplemental Digital Content 4, which shows the Anticoagulation Medication Exposure.

Patient Attributes and Demographics

Patient attributes included sex, age, geographic region, insurance type, income level, and associated comorbidities. Patient comorbidities were stratified using the Elixhauser comorbidity score.²⁰⁻²² ICD-9 codes were used to examine all health care claims for the presence of thirty relevant patient comorbidities (See Appendix 5, Supplemental Digital Content 5, which shows the Elixhauser Comorbidity.

Statistical Analysis

We used descriptive statistics to summarize the characteristics of the cohort, including sex, age, median income, region, comorbidities, smoking status, type of surgery, anticoagulation medications within 30 days after operation, and treatment with IV forms of antibiotics within 30 days after surgery. Given the size of the sample, we used standard differences to examine the baseline characteristics between patients receiving ketorolac within 48 hours after surgery compared to patients not receiving ketorolac. A difference of less than 0.1 was used to indicate a negligible difference in the mean or prevalence of a covariate between treatment groups.²³ We calculated the standard difference in addition to the chi square test because sample size influences the P value even though the difference is very small between two groups. We used logistic regression to calculate an odds ratios (OR) to identify the complication risk associated with perioperative ketorolac use. Covariates for logistic regression were selected based on significant differences between groups in univariate statistics and for specific conditions known to be associated with the outcome under analysis. For example, hematoma was used as a covariate for seroma, but both hematoma and seroma were excluded as covariates for reoperation as these are both potential causes for this outcome. Fisher exact test was to calculate differences in readmission diagnoses. We also calculated the adjusted OR with adjustment for age, sex, median income, region, Elixhauser comorbidity score, hypertension, deep venous thrombosis (DVT), pulmonary embolism (PE), tobacco use, other anticoagulation (clopidogrel, enoxaparin, warfarin, heparin, aspirin), surgery type, and hematoma when looking at other outcomes. All tests were performed using a 2-sided significance level for a P value of 0.05.

RESULTS

Study Cohort

The total cohort was 106,279 patients after all exclusion and inclusion criteria were satisfied. Of these, 4,924 patients (4.6%) received perioperative ketorolac whereas 101,355 (95.4%) received no ketorolac (Table 1). The study demographic had a few baseline differences. The cohort receiving ketorolac demonstrated a small difference in age (45.2 years vs 47.6 years; SD = 0.21; P <0.001). Ketorolac patients had a small difference in annual income (mean

income \$52.1k vs \$53.0k; SD = 0.19; $P < 0.001$). Finally, patients receiving ketorolac had a small difference in specific operations performed (21.4% vs 14.7% lipectomy; 76.7% vs 77.5% breast reduction; 1.9% vs 7.9% head/neck procedures; SD = 0.32; $P < 0.001$). Patients receiving ketorolac were geographically more likely to be in the northeast or north central United States ($P < 0.001$), but this was negligible by standard difference (SD = 0.099). There was a small difference between patient comorbidities by Elixhauser comorbidity scoring with ketorolac patients tending to have a higher comorbidity score (SD = 0.049; $P = 0.008$). A small difference in rate of hypertension was noted between the groups (26.3% vs 29.3%; SD = 0.068; $P < 0.001$). Smoking was more common in patients receiving ketorolac (6.2% vs 3.9%; SD = 0.10; $P < 0.001$). Overall, the cohort was similar with respect to receiving anticoagulation postoperatively, comorbid conditions, and gender.

Risk for Complications and Reoperation

A small difference in absolute risk of ICD-9 diagnosis of hematoma was noted for patients receiving ketorolac vs the control group (2.3% vs 1.7%; $P = 0.002$) and a number needed to harm calculation suggests that over 172 patients would require ketorolac prior to the incidence of an additional hematoma event (Table 2). Hematoma occurred more frequently in patients receiving ketorolac compared to controls within 72 hours of surgery (1.2% vs 0.9%; $P = 0.036$) and between 3 to 30 days after surgery (1.2% vs 0.9%; $P = 0.036$). There was a small difference in risk for seroma in the ketorolac group (2.1% vs 1.5%; $P < 0.001$) and a number needed to harm calculation of 167 patients. For acute kidney injury (0.1% vs 0.2%; $P = 0.09$), need for a blood transfusion (0.1% vs 0.1%; $P = 0.51$), or myocardial infarction (0.02% vs 0.04%; $P = 0.72$) within 30 days of surgery, there was no significant difference between ketorolac compared to controls. There was a significant difference in rates of readmission favoring ketorolac (adjusted OR 0.53; 95 percent CI, 0.28 to 0.99). A multivariable logistic regression analysis was performed for rates of hematoma and seroma (Table 3). No significant difference was detected for hematoma within 30 days of surgery (adjusted odds ratio, 1.20; 95 percent CI, 0.99 to 1.46). In multivariable regression, seroma was more common with ketorolac use (adjusted odds ratio 1.28; 95 percent CI, 1.05 to 1.57).

Reoperation for any reason within 72 hours of surgery was more frequent in patients receiving ketorolac compared to control (2.5% vs 1.8%; $P < 0.001$). After multivariable regression, this effect remained significant (OR 1.22; 95% CI, 1.00-1.49; $P < 0.05$) with a number needed to harm of about 262 patients prior to a reoperation event. Reoperation for a diagnosis of hematoma was also more common with ketorolac, but the absolute difference was small (0.6% vs 0.4%; $P = 0.009$). In contrast, the ketorolac group was readmitted to the hospital less frequently compared to the control group (3.1% vs 5.0% percent; $P < 0.001$). The rate of readmission with either a primary or secondary diagnosis of pain was reduced in patients receiving IV ketorolac (0.6% vs 4.3%; $P = 0.021$). The average insurance reimbursement for reoperation in our cohort was \$1,067. The average readmission cost was \$4,547 per day across the cohort with a mean duration of admission of 4.4 days for the control group and 3.2 days for the ketorolac. On average, patients receiving ketorolac saved \$157 for their care. If applied across the cohort, this would have reduced healthcare expenditure by over \$16 million in this cohort.

Ketorolac Dose-Dependent Rates of Complication

Patients were subdivided into 15mg versus 30mg or greater doses of ketorolac (Table 4). Most patients received only 15mg of ketorolac (89.1%) whereas a minority received higher dosing (10.9%). For low dose versus high dose ketorolac, there was no difference in rate of hematoma (2.2% percent vs 2.9%; $P = 0.30$) or reoperation (2.5% vs 2.1%; $P = 0.52$). There was no difference in rates of renal complications (0.2% vs 0.0%; $P = 0.35$) or need for blood transfusion (0.2% vs 0.2%; $P = 0.61$) related to higher doses of ketorolac.

DISCUSSION

Our data suggest that when controlling for demographics and patient comorbidities, there is no difference in rate of hematoma with ketorolac use. However, prior to multivariable regression, a small absolute difference in the risk for hematoma was noted (1.2% vs 0.9%, $P = 0.036$; number needed to harm 424 patients). Ketorolac was also associated with a small increase in risk for reoperation for any cause within 72 hours. Within 72 hours of surgery, the most likely reason for reoperation would most likely be for hematoma, but we cannot rule out ketorolac use in some of these cases as additional analgesia in the setting of multiple operations. By number needed to harm calculations, over 262 patients would need to be treated with ketorolac before incurring any additional operation. This suggests that even though a subtle difference may exist, the effect of this difference is likely of minimal clinical importance. In contrast, patients who did not receive ketorolac were significantly more likely to require readmission to the hospital and had longer hospital stays. Finally, at least one prior study demonstrated a higher rate of hematoma in breast reduction with delivery of 30mg of intravenous ketorolac in recovery.¹⁴ In our cohort, we found no difference in rates of hematoma between low (15mg) or high (30mg) doses of ketorolac.

To date, there is little population-based evidence regarding the risk of postoperative complications and the safety of ketorolac in perioperative care. One meta-analysis found no difference in bleeding with ketorolac, but this meta-analysis combined primary studies across a broad spectrum of surgical fields with variable risks for bleeding.⁸ Another recent systematic review considered primary studies in plastic surgery with multiple routes of ketorolac administration and found that the medication was generally safe in aesthetic procedures.¹¹ For this study, we chose to focus on breast reduction and body contouring given the large surface area involved in the surgical field and the relatively high risk for hematoma in this population. Body contouring is particularly susceptible to hematoma formation and postoperative hematoma is a catastrophic complication when unnoticed. For example, a recent nationwide cohort of post-bariatric abdominoplasty patients had a rate of post-operative blood transfusion of 9.3 percent. This example highlights both the potential rate of hematoma and volume of blood loss that can occur in breast or body contouring procedures.¹⁸

Our cost analysis estimates the average cost difference for ketorolac use across the entire cohort to be a savings of approximately \$157 per patient or over \$16 million in total. This figure considers the difference in cost given the odds of both reoperation and readmission events. Given the push towards bundled payments and changes in healthcare payer characteristics, ketorolac appears to have a practical savings that will save the average

patient both time in the hospital and overall cost. Though not a focus of this analysis, NSAIDs have been shown across multiple studies to be effective in multi-modal analgesia. There could be additional ketorolac-related cost reduction if multimodal analgesia results in fewer narcotic refills. New persistent opiate use after surgery has rates between 5-7% in both minor and major surgical procedures.²⁴ The need for alternative medications has become even more pressing given national attention for the so-called “opioid crisis.”²⁵ Use of non-narcotic medications, like ketorolac, may help to further reduce the overall need for narcotics.

Interestingly, our data do suggest an increased rate of reoperation in patients who do develop a postoperative hematoma. Reversible COX inhibitors, like ketorolac, have no *in vitro* or *in vivo* evidence for thrombolytic potential.²⁶ However, thromboxane inhibition with NSAIDs may reduce platelet aggregation. Thus, once hemostasis is lost, a higher percentage of patients may progress to hematoma requiring surgical washout. Loss of platelet aggregation is illustrated well in one study that showed a benefit to ketorolac use during lower extremity free flap reconstruction.¹⁶ This study showed fewer thrombotic flap complications with ketorolac use and no difference in hematoma rate. However, unlike anticoagulants, ketorolac is unlikely to cause a hematoma directly though it may propagate the effects of hemostasis loss. We did not see any difference in DVT/PE diagnoses rates between the groups, but these complications are rare in outpatient surgery. Another finding without a clear physiologic etiology is the increased rate of seroma seen with ketorolac compared to the control group. We found a higher rate of seroma, even when adjusting for concomitant hematoma. There is no prior link known between seroma and NSAID use and, therefore this finding should not be taken as proof of causality. Furthermore, even if true, the odds of a patient having a seroma compared with control (OR 1.28) was low with over 247 patients requiring intervention before incurring an additional seroma by number needed to harm calculation. Physiologically, this could be related to the reduction in the inflammatory response; likely due to the interstitial physiology associated with leukotriene-mediated increased vascular permeability.²⁶ Interestingly, wound healing problems were not different between the two groups despite the difference in seroma rates. These new considerations regarding peri-operative ketorolac use will require further research to clarify.

This study has several limitations. The MarketScan database provides an incomplete glimpse of enrolled patients over the 5-year sample period. Interactions that do not involve billing may be incomplete and there are a limited number of patient-specific demographics that can be obtained. Additionally, inpatient records within the data set are incomplete because the use of procedural medication injection ‘Jcodes’ (e.g. J-1885, billing code for ‘Injection, ketorolac tromethamine, per 15 mg’) are not consistently used in the inpatient setting as inpatient medications may be bundled in the cost of the admission. Facial rejuvenation, breast reduction, or body contouring procedures are often performed in the outpatient setting and, therefore, we limited the study to outpatient operations. Prescription coverage plans are also variable in coverage for typical over-the-counter NSAIDs, such as ibuprofen or naproxen, and use of these potentially confounding medications was difficult to track in this dataset. However, the data did allow for tracking the timing of IM/IV ketorolac injection, approximate dosage, and subsequent complications incurred by the patient. Additionally, the conclusions are likely strengthened as surgeons refusing ketorolac postoperatively are also

more likely to discourage over-the-counter NSAIDs for the same reasons. The study is also limited in the ability to show causality of complications after medication delivery. For example, ketorolac may be given to a patient for pain and cause a hematoma or, conversely, the increased pain of the hematoma may necessitate the ketorolac to aid in analgesia. Given the baseline worry for increased bleeding risk of ketorolac, it may be safe to assume that ketorolac is more likely causal than confounding in this hypothetical scenario, but a definitive conclusion is not possible. Finally, this study only evaluates the intravenous administration of systemic ketorolac. Thus, the study has limited predictive power for other formulations, including topical, subcutaneous, or oral forms.

Overall, this large, national database study shows no correlation between ketorolac use and ICD-9 diagnosis of hematoma on multivariable logistic regression analysis. There was a small increased risk for reoperation within 72 hours of surgery, but over 262 patients would require treatment with ketorolac prior to any event. Given the small absolute size of the effect and number needed to harm, this effect is likely clinically unimportant. There was a small increased risk for seroma formation postoperatively, but no other evidence exists linking NSAIDs to seroma physiologically so we cannot interpret this finding for causality. Furthermore, ketorolac use reduced the risk and duration of readmission to the hospital with an estimated cost savings of over \$16 million across the cohort. Given ongoing concerns regarding opioid medications and the apparent safety of ketorolac in the surgical setting, ketorolac should be considered in outpatient facial rejuvenation, breast reduction, and body contouring procedures once surgical hemostasis is obtained.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Study Cohort Attrition Diagram.

Table 1

Patient Characteristic and Demographic data

	Total cohort	Perioperative Ketorolac Use		SD	P Value
		No	Yes		
Total (%)	106,279	101,355 (95.4)	4,924 (4.6)	--	--
Age					
Mean age $\pm$ SD	47.5 $\pm$ 13.7	47.6 $\pm$ 13.7	45.2 $\pm$ 12.8	-0.18	<0.001
Sex, n (%)					
Male	7,163 (6.7)	6,856 (6.8)	307 (6.2)	0.078	0.15
Female	99,116 (93.3)	94,499 (93.2)	4,617 (93.8)		
Annual Median Income, n (%) *					
< \$40k *	996 (0.9)	992 (1.0)	4 (0.1)	0.19	<0.001
\$40k - \$50k *	38,309 (36.1)	36,396 (35.9)	1,913 (38.9)		
\$50k - \$60k *	33,506 (31.5)	31,868 (31.4)	1,638 (33.3)		
\$60k - \$70k *	12,357 (11.6)	11,947 (11.8)	410 (8.3)		
> \$70k *	3,726 (3.5)	3,611 (3.6)	115 (2.3)		
Unspecified	17,385 (16.4)	16,541 (16.3)	844 (17.1)		
Mean income $\pm$ SD	52,988 $\pm$ 8738	53,032 $\pm$ 8766	52,073 $\pm$ 8091	-0.11	<0.001
Region, n (%)					
Northeast	19,235 (18.1)	18,267 (18.0)	968 (19.7)	0.099	<0.001
North Central	24,907 (23.4)	23,611 (23.3)	1,296 (26.3)		
South	42,118 (39.6)	40,282 (39.7)	1,836 (37.3)		
West	18,133 (17.1)	17,377 (17.1)	756 (15.4)		
Unspecified	1,886 (1.8)	1,818 (1.79)	68 (1.4)		
Elixhauser Comorbidity score, n (%)					
0	48,723 (45.8)	46,539 (45.9)	2,184 (44.4)	0.049	0.008
1-3	11,318 (10.7)	10,727 (10.6)	591 (12.0)		
4-8	29,341 (27.6)	27,990 (27.6)	1,351 (27.4)		

	Total cohort	Perioperative Ketorolac Use		SD	P Value
		No	Yes		
Total (%)	106,279	101,355 (95.4)	4,924 (4.6)	--	--
>8	16,897 (15.9)	16,099 (15.9)	798 (16.2)		
Other Comorbidities, n (%)					
Hypertension	31,025 (29.2)	29,731 (29.3)	1,294 (26.3)	-0.068	<0.001
DVT	384 (0.4)	370 (0.4)	14 (0.3)	-0.014	0.36
Pulmonary embolism	280 (0.3)	268 (0.3)	12 (0.2)	-0.004	0.78
Tobacco use, n (%)	4,298 (4.0)	3,994 (3.9)	304 (6.2)	0.10	<0.001
Anticoagulation within 30 days postoperatively, n (%)					
Yes	1,840 (1.7)	1,193 (1.2)	53 (1.1)		0.54
Surgery type, n (%)					
Lipectomy	15,899 (15.0)	14,845 (14.7)	1,054 (21.4)	0.32	<0.001
Breast Reduction	82,311 (77.5)	78,534 (77.5)	3,777 (76.7)		
Head/Neck	8,069 (7.6)	7,976 (7.9)	93 (1.9)		

* Values are abbreviated. For example, actual ranges are <\$39,999, \$40,000 - \$49,999, etc

Table 2

Complications and Ketorolac Use

	Entire cohort (n=106,279)	Perioperative Ketorolac Use		P Value	NNT/H [†]
		No (n=101,355)	Yes (n=4,924)		
Reoperation					
<i>Within 72 hours</i>					
All cause	1,921 (1.8)	1,798 (1.8)	123 (2.5)	<0.001	138
Hematoma	408 (0.4)	378 (0.4)	30 (0.6)	0.009	424
<i>Between 3 and 30 days</i>	2,024 (1.9)	1,918 (1.9)	106 (2.2)	0.19	384
Readmission					
<i>Within 30 days</i>					
% readmitted for pain	5,191 (4.9)	5,037 (5.0)	154 (3.1)	<0.001	54
Mean length of stay (days)	217 (4.3)	216 (4.3)	1 (0.6)	0.021	27
	4.3 days	4.4 days	3.2 days		
Postoperative Office Visits*					
Global period (0-90 days)	533 (0.5)	512 (0.2)	21 (0.4)	0.45	
Complications					
<i>Within 72 hours</i>					
Hematoma	978 (0.9)	919 (0.9)	59 (1.2)	0.036	343
<i>Between 3 and 30 days</i>					
Hematoma	959 (0.9)	901 (0.9)	58 (1.2)	0.036	562
<i>Within 30 days after surgery</i>					
Hematoma	1,850 (1.7)	1,737 (1.7)	113 (2.3)	0.002	174
Seroma	1,599 (1.5)	1,495 (1.5)	104 (2.1)	<0.001	167
Cellulitis	4,935 (4.6)	4,722 (4.7)	213 (4.3)	0.28	
Wound Healing	4,293 (4.0)	4,117 (4.0)	176 (3.6)	0.09	
Myocardial Infarction	46 (0.04)	45 (0.04)	1 (0.02)	0.72	
Acute Kidney Injury	222 (0.2)	217 (0.2)	5 (0.1)	0.091	
Blood Transfusion	121 (0.1)	114 (0.1)	7 (0.1)	0.51	
<i>Between 30 and 90 days after surgery</i>					
Hematoma	276 (0.3)	269 (0.3)	7 (0.1)	0.097	

	Entire cohort (n=106,279)	Perioperative Ketorolac Use		P Value	NNT/H [‡]
		No (n=101,355)	Yes (n=4,924)		
Seroma	988 (0.9)	929 (0.9)	59 (1.2)	0.044	356
Cellulitis	2,962 (2.8)	2,836 (2.8)	126 (2.6)	0.32	
Wound Healing	3,267 (5.9))	3,134 (3.1)	133 (2.7)	0.12	
Myocardial Infarction	45 (0.04)	45 (0.04)	0 (0.0)	0.27	
Acute Kidney Injury	169 (0.2)	163 (0.2)	6 (0.1)	0.50	

* Office visits in the global period tracked by CPT 99024

[‡] NNT/H, patient number needed to treat / harm (patients who would need to receive treatment (instead of control) to achieve this benefit or complication

Table 3

Multivariable Analysis of Ketorolac Use and Complications

Postoperative Outcomes	Ketorolac Use	Adjusted odds ratio (95% CI)		
Hematoma within 30 days	No	1	Reference	
	Yes	1.20	(0.99-1.46)	
Seroma within 30 days^a	No	1	Reference	NNH [‡]
	Yes	1.28	(1.05-1.57) *	247 patients
Reoperation within 72 hours	No	1	Reference	NNH [‡]
	Yes	1.22	(1.00-1.49) *	262 patients
Readmission within 30 days	No	1	Reference	NNT [‡]
	Yes	0.76	(0.62-0.93) *	87 patients

Adjusted for age, sex, median income, region, Elixhauser comorbidity score, hypertension, deep venous thrombosis, pulmonary embolism, tobacco use, postoperative anticoagulation, surgery type.

^a Seroma was independently controlled for concomitant hematoma

[‡] NNH, number needed to harm; NNT, number needed to treat

* P < 0.05

Table 4**Ketorolac Dosing and Complication Risk**

	Ketorolac		P Value
	15mg (n = 4,092)	30 mg (n = 583)	
Reoperation			
Within 72 hours			
All cause	102 (2.5)	12 (2.1)	0.52
Hematoma	25 (0.6)	2 (0.3)	0.57
Between 3 and 30 days	85 (2.1)	14 (2.4)	0.61
Complication			
Within 72 hours			
Hematoma	49 (1.2)	6 (1.0)	0.72
Within 30 days after surgery			
Hematoma	91 (2.2)	17 (2.9)	0.30
Seroma	91 (2.2)	7 (1.2)	0.11
Cellulitis	172 (4.2)	29 (5.0)	0.39
Myocardial Infarction	1 (0.02)	0 (0.0)	1.00
Acute Kidney Injury	5 (0.1)	0 (0.0)	1.00
Blood Transfusion	6 (0.2)	1 (0.2)	0.61
Between 30 and 90 days after surgery			
Hematoma	4 (0.1)	2 (0.3)	0.17
Seroma	40 (1.0)	10 (1.7)	0.11
Cellulitis	96 (2.4)	18 (3.1)	0.28
Myocardial Infarction	0 (0.0)	0 (0.0)	--
Acute Kidney Injury	6 (0.2)	0 (0.0)	0.35