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Opioid Prescribing Patterns, Patient Use, and Postoperative Pain After Benign Hysterectomy

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Abstract

Objective—To quantify physician prescribing patterns and patient opioid use in the two weeks after hysterectomy at an academic institution, and determine whether patient factors predict postsurgical opioid use and pain recovery.

Methods—We conducted a prospective quality initiative study by recruiting all English-speaking patients undergoing hysterectomy for benign, non-obstetric indications at a university hospital between August and December 2015, excluding those with major medical morbidities or substance abuse. Before hysterectomy, patients completed the Fibromyalgia Survey, a validated measure of centralized pain. Following hysterectomy, opioid use (converted to oral morphine equivalents) and pain scores (0–10 numeric rating scale) were collected by a daily diary and a structured telephone interview 14 days after surgery. Primary outcomes were total opioid prescribed and consumed in the 2 weeks after hysterectomy. Secondary outcomes included daily opioid use and daily pain severity for 14 days after hysterectomy.

Results—Of 103 eligible patients, 102 (99%) agreed to participate, including 44 (43.1%) laparoscopic, 42 (41.2%) vaginal, and 16 (15.7%) abdominal hysterectomies. Telephone surveys were completed on 89 (87%) participants, diaries were returned from 60 (59%) participants. Diary non-responders had different baseline characteristics than non-responders. Median amount of opioid prescribed was 200 oral morphine equivalents (interquartile range (IQR) 150–250). Patients reported using approximately half of the opioids prescribed, with a median excess of 110 morphine equivalents (IQR 40–150). The best fit model of total opioid consumption identified preoperative Fibromyalgia Score, overall body pain, preoperative opioid use, prior endometriosis, abdominal hysterectomy (compared to laparoscopic), and uterine weight as significant predictors.

Highest tertile of Fibromyalgia Score was associated with greater daily opioid consumption (13.9 [95% CI 3.0 – 24.8] greater OME at baseline, $p=0.02$).

Conclusion—Gynecologists at a large academic medical center prescribe twice the amount of opioids than the average patient uses after hysterectomy. A personalized approach to prescribing opioids for postoperative pain should be considered.

Introduction

Opioid misuse and abuse has been described by the US Centers for Disease Control and Prevention as one of the top five public health threats in 2016.¹ While providing adequate postoperative pain control has been deemed a fundamental right,² surgeon overprescribing has been implicated in opioid diversion, potentially fueling the opioid epidemic.³ Thus, surgeons must find the best balance between over- and under-prescription, highlighting the need for improved and personalized postoperative opioid prescribing guidelines. Currently, there are no evidence-based guidelines to inform surgeons on appropriate opioid prescribing for the management of postsurgical pain.

Recent studies have found that most patients undergoing various surgical procedures^{4–7}, including cesarean section^{8,9}, are prescribed opioids in excess of what they use. Despite the era of personalized medicine, most studies did not investigate whether individual patient factors influence opioid use and postsurgical pain during the postoperative period. These data are critical for the development of evidence-based opioid prescribing guidelines tailored to individual patient characteristics. Hysterectomy is the most common surgical procedure performed in non-pregnant women^{10,11}, making this a critical target for improvement in opioid prescribing. As part of a quality initiative project, we sought to prospectively quantify physician prescribing patterns and patient opioid use in the first two weeks after hysterectomy for benign indications. Our secondary aim was to determine whether individual patient and surgical factors predict patterns of postsurgical opioid use and pain after hysterectomy.

Materials and Methods

The institutional review board at the University of Michigan determined that this quality initiative project was exempt and provided approval for publication because our study did not fit the definition of human subjects research requiring IRB approval. All consecutive, English-speaking patients scheduled for hysterectomy for a benign indication at a single, university hospital from August 31st to December 18th, 2015 were prospectively recruited on the day of surgery. Women with a cancer or obstetric indication, medical comorbidity that significantly altered postoperative opioid management, history of opioid addiction or substance abuse were excluded. Patients were informed that this quality initiative involved completing a brief set of questionnaires prior to surgery, a pain and medication daily diary for 14 days after surgery, and a brief telephone survey approximately 14 days after surgery. The primary outcomes were total opioid prescribed by the surgeon and total opioid consumption in the 2 weeks after hysterectomy. Secondary outcomes included daily opioid use and daily postoperative pain severity scores in the 2 weeks after hysterectomy.

In the preoperative holding area, patients completed brief standardized validated self-report measures of pre-surgical pain, associated somatic symptoms, and preoperative opioid use. The primary predictor of interest was the 2011 Fibromyalgia Survey Score (Fibromyalgia Score)¹², which is the sum of the total number of painful body areas (0 to 19 points) and the severity of fatigue, trouble thinking, and headaches (0 to 12 points). This measure has demonstrated good reliability, convergent and discriminant validity, and has been used as a continuous measure to assess the degree of “centralized pain”^{12,13}, defined as any central nervous system dysfunction that plays a role in pain amplification.¹⁴ Centralized pain disorders are characterized by widespread pain and co-occurring somatic symptoms, such as fatigue, sleep and memory difficulties.¹⁴ The Fibromyalgia Score has been shown to be highly predictive of acute postsurgical opioid use during hospitalization among patients undergoing hysterectomy or knee or hip arthroplasty.^{15,16} Patients also completed self-report measures of average pelvic and overall body pain in the month prior to surgery using an 11-point numeric rating scale (NRS) with 0 indicating “no pain” and 10 indicating “pain as bad as you can imagine.” Patients were classified as “preoperative opioid user” if they reported using opioids more than once per week for any reason in the month prior to hysterectomy.

A standardized case report form was used to abstract patient and surgical characteristics from the electronic medical record by a gynecologist (SA, ST, or EM) blinded to the study results. We focused on characteristics prior to hospital discharge, as these would be the available data that could be used to develop postoperative opioid prescription guidelines. Demographic and medical history included age (years), race (white or non-white), current smoking status, current use of medications for depression, anxiety or neuropathic pain. Indications for hysterectomy were determined by review of operative report and outpatient clinic visits. Patients could have more than one indication for hysterectomy, and these diagnoses were not considered mutually exclusive except for dysmenorrhea and chronic pelvic pain. Dysmenorrhea was defined as pelvic pain that occurred primarily during menstruation, and chronic pelvic pain was defined as non-cyclic pelvic pain that was not limited to the time of menstruation. Route of surgery was categorized as abdominal, vaginal, or laparoscopic (which included traditional and robot-assisted laparoscopy). Additional surgical procedures performed at the time of hysterectomy were noted. When identified, endometriosis was assigned a stage according to the revised American Fertility Society endometriosis scoring system.¹⁷ Adhesions were scored using the validated scoring system developed by the Adhesion Scoring Group.¹⁸ The type of opioid, dose, and total number of pills prescribed in the first 14 days since discharge, were obtained from the electronic medical record.

Postoperative opioid use and pain symptoms were collected by a telephone survey on postoperative day 14 and secondarily using daily diaries completed for the first 14 days after hysterectomy. Telephone interviews were conducted using a standardized script. If we were unable to reach the patient on the first attempt, a total of 3 attempts were made. The telephone survey queried the name(s), dose, and total number of opioid pills used since discharge, request for opioid refills since discharge and number of remaining opioid pills. If a patient requested a refill, all patients confirmed that they used all pills in the original prescription. Using daily “diaries”, participants also recorded their average pain (0–10 NRS), and the name, dose, and total number of opioid pills used at the end of each day for

the first 14 days after hysterectomy. The last day of opioid use was determined from completed diaries. All opioid data used in this study was converted to oral morphine equivalents (OME) using the guidelines published by the Center for Disease Control.¹⁹

Data analyses were performed using STATA 14.0 (StataCorp, College Station, TX) and R 3.3.1 (The R Foundation for Statistical Computing). Descriptive data were analyzed using χ^2 or Fisher's exact test where applicable for categorical variables, Student's t-test or one-way analysis of variance (ANOVA) for normally distributed continuous variable, or via nonparametric Wilcoxon Rank-Sum test if the distribution was non-normal. Descriptive statistics on continuous variables showing no significant skewness (d'Agostino test) were reported as mean and standard deviation and statistics on skewed variables were reported as median and interquartile range. To explore the relationship between Fibromyalgia Score, daily opioid use and pain recovery, the cohort was divided into tertiles based on the distribution of the Fibromyalgia Survey Score, as previously described.^{15,16} Mean plots with 95% Confidence Intervals (CI) were generated to demonstrate daily mean opioid consumption and daily mean "average pain" stratified by Fibromyalgia Score tertile in the 2 weeks after hysterectomy.

Multivariate linear regression models were fit to estimate 2-week total opioid consumption. All preoperative covariates were examined for collinearity and considered as possible covariates in the multivariate modeling. We also examined the relationship between preoperative Fibromyalgia Score and daily postoperative pain and opioid use. Longitudinal multivariate analyses of the patterns of pain and opioid consumption during the 2 weeks after hysterectomy were done using linear mixed regression models with normal random intercept term shared by measurements on the same subject. Best models for all analyses were obtained using a backward selection procedure, repeated application of the likelihood ratio test, with results confirmed using Akaike Information Criteria (AIC, BIC). In the longitudinal models, time was represented as a categorical variable to allow enough flexibility to describe the complex dynamics of the pain and opioid responses. Differences between groups based on Fibromyalgia Score were expressed as the main effect of group and the group by time interaction. Plots of residuals were used to confirm no evidence of violations of model assumptions.

Results

During the study period, 108 women underwent hysterectomy for benign indications. Of these, five women were not eligible to participate (one did not speak English, one had renal failure, and three had a history of addiction or buprenorphine use prior to hysterectomy). Of 103 eligible patients, 102 (99%) agreed to participate, including 44 (43.1%) laparoscopic, 42 (41.2%) vaginal, and 16 (15.7%) abdominal hysterectomies. Telephone surveys used to ascertain the primary outcome (total opioid consumption in the two weeks after hysterectomy) were successfully completed on 89 (87%) of participants. Diaries which collected secondary outcomes (daily pain and opioid use) were returned from 60 (59%) of participants (Figure 1). Relative to women who returned their 2-week diary, diary non-responders were younger (44.7 ± 11 . vs 51.8 ± 11.2 years, $p=0.002$), reported higher Fibromyalgia Survey Score (9.7 ± 5.5 vs 5.6 ± 3.6 , $p<0.001$), and were more likely to be

non-white (26.1% vs 10.7%, $p=0.04$), prior opioid user (21.7% vs 3.6%, $p=0.005$), smoker (22.2% vs. 3.6%, $p=0.004$), and have a history of depression (41.3% vs 21.4%, $p=0.03$). Clinical characteristics and intraoperative findings of the sample are summarized in Table 1.

Surgeon prescribing patterns and patient opioid use in the 2 weeks after hysterectomy by route of surgery are reported in Table 2. Overall, the median amount of opioid prescribed upon discharge after hysterectomy at our institution was 200 oral morphine equivalents (OME), equivalent to 40 tablets of 5-mg hydrocodone. However, patients reported using approximately half of the opioids prescribed with a median excess of 110 OME per patient (interquartile range 40–150), equivalent to 22 unused tablets of 5-mg hydrocodone. In the univariate analyses, average opioid use and duration of opioid use in the first two weeks after hysterectomy did not differ significantly according to surgical approach in this sample. Overall, 97% women reported adequate or good postoperative pain control, and approximately 40% felt that they received too much opioid after surgery.

Multivariable linear regression identified 7 factors that best predicted total postoperative total opioid consumption in the 2 weeks after hysterectomy (Table 3). For example, interpretation of this model indicates that each 1-point increase in Fibromyalgia score is associated with 30.8 more OME's used in the 2-weeks after hysterectomy, after controlling for all other variables in the model. Women with a history of endometriosis (but not necessarily those with endometriosis at the time of hysterectomy) used 190.8 more OME in the 2 weeks after hysterectomy, while those who were using medication for neuropathic pain used 178.9 OME less. There was no difference in predicted opioid use when comparing vaginal to laparoscopic hysterectomy. Predictors of total opioid consumption after excluding chronic opioid users were similar to those in the total sample, with preoperative Fibromyalgia Score remaining strongly predictive of total opioid consumption (Table 4).

The mean Fibromyalgia Survey Score prior to hysterectomy was 7.5 ± 5.0 with a range of 0 to 24. The cohort was divided into equal tertiles based on the distribution of the preoperative Fibromyalgia Score (Low: 0 to 4, Moderate: 5 to 10, High, 11–31), as previously described.^{15,16} Average daily postoperative pain and opioid use in the first two weeks after hysterectomy, stratified by tertiles of preoperative Fibromyalgia Score, are shown in Figures 2. Linear mixed regression models confirmed that patients in the highest tertile of Fibromyalgia Score reported significantly higher postoperative opioid consumption each day after hysterectomy (13.9 greater OME at baseline [95% CI 3.0 – 24.8], $p=0.020$) with the difference decreasing by 0.9 OME per day ([95% CI 0.3–1.5], $p=0.002$) relative to patients in the moderate or low Fibromyalgia groups. Furthermore, patients in the highest tertile of Fibromyalgia Score reported significantly higher postoperative average pain scores (2.4 points higher on 0–10 NRS at baseline, [95% CI 0.9 – 4.0], $p=0.00400$); relative to the moderate or low Fibromyalgia groups. While those in the moderate and low Fibromyalgia group reported improvement in pain over time after hysterectomy, the patients in the highest tertile reported worsening pain after surgery (increasing by 0.2 points per day [95% CI 0.1 – 0.3]).

Discussion

We found that gynecologists in a large academic medical center prescribe approximately twice the amount of opioids than the average patient uses after hysterectomy. Individual patient factors that independently predicted two-week opioid consumption after discharge were similar to those we previously reported to predict opioid consumption prior to hospital discharge,¹⁶ and included route of hysterectomy, Fibromyalgia Survey Score, preoperative opioid use, and history (but not presence) of endometriosis.

Reasons for surgeons providing excess opioids are likely multifactorial, and probably relate to lack of evidence-based guidelines on appropriate postoperative opioid prescribing, desire to improve patient satisfaction, and reduce postoperative opioid refill requests. However, recent studies found no association between the amount of opioid prescribed and the likelihood of refill request after surgery²⁰, and no association between the initial postoperative prescription, patient satisfaction⁸, or the Hospital Consumer Assessment of Healthcare Providers and Systems pain measure.²¹ These findings should reassure surgeons that reducing the amount of opioid provided after surgery should still provide adequate pain management while maintaining patient satisfaction in most patients.

Our findings of opioid over-prescription are similar to recent reports in other surgical cohorts⁴⁻⁷, including cesarean section.^{8,9} However, few studies have examined whether individual patient factors predict outpatient opioid use. One recent study reported that individual in-hospital opioid consumption was correlated with post-discharge opioid use.⁹ Similar to our findings, these data support the notion that individual patient factors influence postoperative opioid use and pain, independent of surgical factors. Thus, a “one-size-fits-all” approach to prescription guidelines may miss an important but feasible opportunity to personalize postoperative pain management.

Our findings indicate that a validated, self-report measure of centralized pain, the 2011 Fibromyalgia Survey Score¹², influences patient opioid use and pain recovery after hysterectomy. Centralized pain disorders refer to any chronic pain condition where central nervous system dysfunction plays a role in augmenting and maintaining pain.¹⁴ This phenotype is characterized by multifocal pain and co-occurring somatic symptoms, including fatigue, sleep and mood disturbances. We have previously demonstrated that the Fibromyalgia Score predicts total opioid use during hospitalization after hysterectomy¹⁶ and knee or hip arthroplasty¹⁵, as well as persistent pain 6 months after arthroplasty.²² We now demonstrate this measure is also a strong predictor of total opioid use, time to opioid cessation, and pain recovery in the two weeks after hysterectomy. For example, a woman with a Fibromyalgia Score of 12 (who does not meet diagnostic criteria for fibromyalgia) is predicted to use 300 more OME (i.e. 60 more 5mg hydrocodone pills) in the two weeks after hysterectomy than someone with a score of 2, after adjustment for other covariates. Furthermore, women in the top Fibromyalgia Score tertile used more opioid for longer periods of time, with minimal improvement in pain in the two weeks after hysterectomy. These findings are consistent with published data suggesting opioid non-responsiveness in patients with centralized pain.^{23,24}

Strengths of the study include novel analysis of “centralized pain” as predictor of an individual patient’s postoperative opioid use and prospective data collection in consecutive women undergoing hysterectomy. Despite its strengths, there are several limitations. Data from our large, academic hospital may not be generalizable to other populations and hospital settings. The study group included relatively few abdominal hysterectomies, which limits interpretation of findings in this cohort. Opioid use after discharge was based on self-report, since we do not routinely ask patients to return to clinic for a pill count after surgery. Finally, only about 60% of patients returned their postoperative diaries which provided data for our secondary outcomes. Although this may limit interpretation of daily opioid use and pain scores after hysterectomy, we successfully collected total opioid use on nearly 90% of our participants through telephone surveys. Furthermore, the diary non-responders were more likely to have multiple characteristics that were associated with higher opioid use and pain scores (higher preoperative Fibromyalgia Score and chronic opioid use). Thus our findings likely underestimated the difference in pain and opioid recovery in women with high versus low Fibromyalgia Scores.

The opioid epidemic may be partly fueled by over-prescription of opioids postoperatively.³ While surgeons must adequately control postoperative pain, most surgeons prescribe opioids in excess of the amount women use, making this an important target for improvement for gynecologic surgeons. A personalized approach to prescribing opioids for postoperative pain may be feasible, and should focus on surgical approach and individual patient characteristics, such as measures of centralized pain. Multimodal postoperative analgesia that utilizes opioid and non-opioid strategies should be considered, and may be especially beneficial for patients with centralized pain.²⁵

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Figure 1.

Patient flow diagram and survey response rate per primary and secondary outcome measures. *Telephone survey response rate: n=89/102; 87%. †Daily diary response rate: n=60/102; 60%.

Figure 2.

Mean opioid consumption (**A**) and average pain (**B**) per day after hysterectomy stratified by preoperative fibromyalgia score tertile (low: 0–4 points; moderate: 5–10 points; high: 11–31 points). *Error bars* represent 95% CIs. NRS, Numeric Rating Scale.

Table 1

Preoperative characteristics and intraoperative findings of the study sample.

Preoperative characteristic	All patients (n=102)
Age (years)	48.5 ± 11.67
White Race	84 (82.4)
Body mass index (kg/m ²)	30.1 ± 6.5
Current smoker	12 (11.8)
Current use of medication for depression or anxiety	31 (30.4)
Current use of medication for neuropathic pain	13 (12.8)
Preoperative opioid use	12 (11.8)
History of endometriosis	8 (7.8)
Average overall body pain (0–10 NRS)	2.6 ± 2.6
Average pelvic pain (0–10 NRS)	2.8 ± 3.0
Fibromyalgia Survey Score (0–31)	7.5 ± 5.0
Route of hysterectomy	
Laparoscopic	45 (44.1)
Vaginal	41 (41.2)
Abdominal	16 (15.7)
Indication for hysterectomy *	
Chronic pelvic pain	14 (13.7)
Dysmenorrhea	9 (8.8)
Leiomyomas	32 (31.4)
Abnormal uterine bleeding	47 (46.0)
Prolapse	27 (26.5)
Additional procedures performed with hysterectomy	
Unilateral salpingo-oophorectomy	9 (8.8)
Bilateral salpingo-oophorectomy	15 (14.7)
Tension-free transvaginal tape	12 (11.8)
Prolapse surgery †	26 (25.5)
rAFS endometriosis stage	
0 (no endometriosis)	88 (86.3)
I–II	10 (9.8)
III–IV	4 (3.9)
Diamond adhesion score	0 (0, 23)
Specimen weight (grams)	130 (61.5, 308)

Data are presented as mean ± standard deviation, median (interquartile range), or N (%).

NRS, numeric rating scale; rAFS, Revised American Fertility Society

* Patients can have more than one indication for hysterectomy.

† Prolapse surgery includes anterior repair, posterior repair, uterosacral ligament suspension, sacrospinous ligament suspension, vaginal mesh excision, sacrocolpopexy, colpocleisis.

Table 2

Surgeon prescribing patterns and patient opioid use after hysterectomy.

	All patients (n=102)	Laparoscopic (n=44)	Vaginal (n=42)	Abdominal (n=16)	p-value *
Length of stay (days)	1 (1,3)	1 (1,1)	1 (1,1)	2 (2,3)	<0.001
OME prescribed at discharge	200 (150,250)	200 (200,280)	150 (150,200)	200 (200,300)	0.005
OME used by patient in first 2 weeks	85 (14,165)	70 (15,202)	50 (5,120)	100 (80,150)	0.15
Number of patients who requested refills in first 2 weeks	10 (9,8)	6 (13,3)	4 (9,76)	0 (0)	0.31
Excess OME	110 (40,150)	112 (30,200)	110 (40,150)	105 (50,170)	0.40
Total days of opioid use	5 (1,10)	4 (2,10)	4 (1,8)	9 (5,12)	0.43

Data are presented as median (interquartile range), or N (%)

OME, oral morphine equivalent

* Corresponds to Kruskal-Wallis test (continuous variables) or Wald χ^2 test (categorical variables).

Table 3

Best fit multivariate linear-regression model predicting total postoperative opioid use (oral morphine equivalents) in the 2 weeks after hysterectomy in all patients (fixed effects).

Preoperative characteristic	AdjustedBeta-estimate *	SE	p-value
Intercept	−13.9	40.2	0.73
Current use of medication for neuropathic pain (yes/no)	−178.9	76.5	0.02
Chronic opioid use (yes/no)	322.3	70.3	<0.001
History of endometriosis (yes/no)	190.7	79.2	0.02
Average overall body pain (0–10 NRS)	−34.6	13.0	0.01
Fibromyalgia Survey Score (0–31)	30.8	6.7	<0.001
Route of hysterectomy (abdominal versus laparoscopic)	160.3	71.8	0.03
Specimen weight (grams)	−0.2	0.06	0.02

NRS, numeric rating scale; SE, standard error.

* Based on multivariate linear-regression model adjusted for all variables listed in this table.

Table 4

Best fit linear-regression model of total postoperative opioid consumption (oral morphine equivalents) in the 2 weeks after hysterectomy in opioid naïve patients (fixed effects).

Preoperative characteristic	Beta-estimate	SE	p-value
Intercept	−0.29	26.78	0.99
Current use of medication for neuropathic pain (yes/no)	−141.2	62.19	0.03
History of endometriosis (yes/no)	137.35	50.09	0.01
Average overall body pain (0–10 NRS)	−16.65	8.09	0.05
Fibromyalgia Survey Score (0–31_	17.86	4.43	<0.001
Route of hysterectomy (abdominal vs laparoscopic)	112.47	43.78	0.01
Specimen weight (grams)	−0.14	0.05	0.01
Indication for hysterectomy: dysmenorrhea (yes/no)	135.05	50.08	0.01
Indication for hysterectomy: fibroids (yes/no)	88.11	36.36	0.02

NRS, numeric rating scale; SE, standard error.

* Based on multivariate linear-regression model adjusted for all variables listed in this table.