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Association of Prehabilitation With Postoperative Opioid Use in Colorectal Surgery: An Observational Cohort Study

Angela Lee, MD[a], Elizabeth Shelton, MPH[b], Serena Bidwell, MPH[b], Kreeti Shankar, MPH[b], Kazuo Ando, MD, PhD[c], Brice Gaudilliere, MD, PhD[c], Andrew Shelton, MD[b], Cindy Kin, MD, MS[b,*]

[a]School of Medicine, Stanford University, Stanford, California

[b]Department of Surgery, Stanford University, Stanford, California

[c]Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University, Stanford, California

Abstract

Introduction: Preoperative optimization programs have demonstrated positive effects on perioperative physical function and surgical outcomes. In nonsurgical populations, physical activity and healthy diet may reduce pain and pain medication requirement, but this has not been studied in surgical patients. Our aim was to determine whether a preoperative diet and exercise intervention affects postoperative pain and pain medication use.

Methods: Patients undergoing abdominal colorectal surgery were invited to participate in a web-based patient engagement program. Those enrolling in the first and third time periods received information on the standard perioperative pathway (enhanced recovery after surgery [ERAS]). Those enrolling in the second time period also received reminders on nutrition and exercise (PREHAB + ERAS). The primary outcome was postoperative inpatient opioid use. The secondary outcomes were inpatient postoperative pain scores and nonopioid pain medication use.

Results: The ERAS and PREHAB + ERAS groups were similar in demographic and operative characteristics. Subgroup analysis of patients who activated their accounts demonstrated that the two groups had similar average maximum daily pain scores, but the PREHAB + ERAS group (n = 158) used 15.9 fewer oral morphine equivalents per postoperative inpatient day than the ERAS group (n = 92), representing a 30% decrease (53 mg *versus* 37.1 mg, P = 0.04). The two groups used comparable amounts of acetaminophen, gabapentin, and ketorolac. Generalized linear models demonstrated that PREHAB + ERAS, minimally invasive surgery, and older age were associated with lower inpatient opioid use.

[*]*Corresponding author*. Division of General Surgery, Department of Surgery, Stanford University School of Medicine, 300 Pasteur Drive, H3680K, Stanford CA 94305. Tel.: +1 650 646 0014; fax: +1 650 725 0791. cindykin@stanford.edu (C. Kin).

Author Contributions

A.L. contributed to data acquisition/analysis, drafting, and final approval. E.S., S.B., and K.S. contributed to data acquisition/analysis, critical revision, and final approval. K.A., B.G., and A.S. contributed to analysis and interpretation of data, critical revision, and final approval. C.K. contributed to study conception and design, data analysis/interpretation, drafting and critical revisions, and final approval.

Disclosure

None declared.

Conclusions: Access to a web-based preoperative diet and exercise program may reduce inpatient opioid use after major elective colorectal surgery. Further studies are necessary to determine whether the degree of adherence to nutrition and physical activity recommendations has a dose-dependent effect on opioid use.

Keywords

Prehabilitation; Postoperative opioids; Postoperative pain; Patient engagement; Web-based patient platform

Introduction

The postoperative period is a particularly vulnerable time for the development of opioid dependence. In particular, previously opioid-naïve patients undergoing abdominal operations, such as open and laparoscopic cholecystectomies, open appendectomies, and cesarean deliveries, appear to be at an increased risk for prolonged opioid use and dependence.[1] Several strategies have successfully reduced postoperative opioid use and the risk of dependence, including minimally invasive surgical approaches and implementation of enhanced recovery after surgery (ERAS) clinical protocols.[2] ERAS protocols emphasize multimodal opioid-sparing pain regimens. In some practices, this strategy has led to decreased inpatient opioid use and decreased proportion of patients discharged with opioid prescriptions.[3]

It is unclear whether preoperative interventions may decrease postoperative pain or opioid use. Prehabilitation programs were developed to address the problem of frailty and poor physical function before surgery, as these were risk factors for poor outcomes.[4,5] Some programs have demonstrated success in improving functional outcomes in patients undergoing major abdominal surgery.[6-8] In patients undergoing abdominal surgery, prehabilitation has already been associated with improved postoperative outcomes, such as decreased postoperative delirium,[9] improved walking capacity,[7] strength, endurance,[10] and time needed to return to baseline capacity,[7] and stress.[10] Preoperative weaning of opioids has been advocated as an important component of prehabilitation that would decrease postoperative opioid use and dependence, but this strategy is not widely practiced.[11]

One outcome of prehabilitation that has not been explored is its effect on pain and opioid use. There is some evidence to suggest that exercise and improved diet quality reduce the perception of pain in some patient populations.[12-15] The aim of this study is to determine whether implementation of a preoperative nutrition and exercise remote coaching program would be associated with differences in postoperative pain and opioid use. Our hypothesis was that patients who underwent prehabilitation would experience less postoperative pain and require lower doses of opioid medications.

Methods

This observational cohort study followed all patients scheduled for major elective colorectal surgery who agreed to enroll in a web-based platform (SeamlessMD, Toronto) during the perioperative period, starting in October 2017. The purpose of the online program was to improve patient engagement with the standard ERAS clinical pathway and improve patient comprehension of the large amount of information that they normally receive at the time of surgical consultation. The program was accessible online via computer or mobile application and contained standard preoperative instructions such as cessation of anticoagulant medications, bowel preparation and oral antibiotics, and fasting guidelines. It also contained standard information on what to expect in the immediate postoperative period as part of the standard ERAS clinical pathway such as urinary catheter removal and importance of walking. Instead of the patient receiving all this information in one packet at the preoperative surgical consultation, they received this information at the relevant time points in the form of notifications from the mobile application or web portal. Patients were prompted to log completion of tasks, such as taking oral antibiotics the day before surgery or walking at least three times on the days after surgery.

In May 2018, we added a prehabilitation component to the web-based platform. This preoperative nutrition and exercise program consisted of a customizable daily step goal, strength exercises, and nutrition guidance to consume at least five fruits and vegetables per day, two servings of fiber-rich whole-grain foods, and two servings of plant protein, while limiting consumption of added sugars and saturated fats. Patients who were on specialized diets were referred to a registered dietician. Patients received pedometers so that they could log their steps in the web-based platform. The program delivered electronic reminders to follow the program in addition to the standard ERAS-related reminders. Eligibility criteria included patients who are 18+ y old undergoing major surgery in 3+ wk, who had an internet-enabled device. From April 2019 to June 2019, patients continued to be invited to participate in the original online program that focused only on the ERAS protocol, without the prehabilitation component. Patient demographic information, surgical indication, operative data, postoperative pain scores, and pain medication use were collected from the electronic medical record (Fig. 1). The Stanford University institutional review board approved the prehabilitation program protocol for which patients gave informed consent and approved the retrospective analysis of all patients included in this analysis with a waiver for informed consent.

The primary outcome was average daily inpatient opioid use measured as oral morphine equivalents.[16,17] Total daily doses of opioid medications were converted to oral morphine equivalents for up to five inpatient days, and an average daily dose was calculated based on the length of stay. The secondary outcomes were postoperative inpatient maximum pain scores and use of nonopioid pain medications including ketorolac, gabapentin, and acetaminophen. The comparison groups were patients who were enrolled in the web-based program that included the prehabilitation component from May 2018 to May 2019 (PREHAB + ERAS) *versus* those who were enrolled in the web-based program that did not include the prehabilitation program (ERAS).

Univariate analyses were performed for demographic and operative characteristics between ERAS and PREHAB + ERAS groups. Distribution of data was assessed with visual analysis of histograms. We used two-sided *t*-tests for normally distributed continuous variables, the Wilcoxon rank-sum test for non-normally distributed continuous variables, and χ^2 tests for categorical data (Stata/SE 16.1, College Station, TX). The same was carried out for each of the primary and secondary outcomes. Multivariable linear regression was performed for each of the primary and secondary outcomes, controlling for age, sex, and surgical approach (open *versus* minimally invasive). Generalized linear models were used to analyze outcomes with a non-Gaussian distribution.

To determine whether there was a secular trend toward lower opioid use over the entire study period, we averaged patient data by month over the first time period (ERAS-only) and the third time period (ERAS-only). We excluded the second time period (PREHAB + ERAS) because this time period involved the prehabilitation intervention. We used a generalized linear model to account for the gamma distribution of these data to determine if time (by month) was an independent factor.

To determine if engagement and adherence to the prehabilitation program were associated with opioid use within the PREHAB + ERAS group, we performed a subset analysis of the data collected via the online platform. We defined the level of engagement with the program as the number of days they used the program to log daily exercises as a proportion of days that they had access to the program and the number of weeks they completed dietary recall surveys as a proportion of weeks that they had access to the program. We used generalized linear models to account for the gamma distribution of the primary outcome, average daily postoperative opioid use, adjusting for exercise-related engagement or diet-related engagement, age, sex, and surgical approach. Exercise-related adherence was defined as the proportion of days logging physical activity on which the subjects walked more than 5000 steps or did strength exercises. Diet-related adherence was defined as the proportion of days that subjects self-reported consuming at least five fruits and vegetables, at least two servings of high-fiber whole-grain foods, at least two servings of plant protein, or avoided added sugar or foods high in saturated fats. We used generalized linear models for each of these independent variables to account for the gamma distribution of the primary outcome, adjusting also for age, sex, and surgical approach. In the surveys given at 30 d after surgery, patients were asked whether they agreed with the following statements: “The walking program I did before surgery helped me recover,” “The strength exercises I did before surgery helped me recover,” and “The changes I made to my diet before surgery helped me recover.” We used generalized linear models to determine if agreement with any of these statements was associated with postoperative opioid use.

Results

There were 132 patients in the ERAS-only group and 205 patients in the PREHAB + ERAS group. The groups were similar in sex, age, body mass index, surgical indication, surgical approach, and mean length of stay (Table 1). There was no statistical difference in the surgical indications and surgical approaches between the two groups.

Of all patients who agreed to sign up with the web-based platform, 26% never activated their accounts. There was no significant difference in the proportion who activated their accounts between the ERAS and PREHAB + ERAS groups (69.7% *versus* 76.7%, $P = 0.49$). The likelihood of activating the platform was not associated with age, diagnosis, or operative approach.

Univariate analysis of the entire cohort, regardless of account activation status, demonstrated that the PREHAB + ERAS group used 13.1 fewer oral morphine equivalents (OMEs) per postoperative inpatient day than the ERAS group, representing a 25% decrease from the ERAS group (52.3 mg *versus* 39.2 mg, $P = 0.049$). There was a 30.9% difference in total OMEs between the ERAS and PREHAB + ERAS groups (220 mg *versus* 152 mg, $P = 0.03$). Patients who underwent an open surgical approach used more opioids per day than those who underwent a minimally invasive approach (55.4 mg *versus* 35.8 mg, $P = 0.003$). There was no difference in opioid use between the sexes. Older age was associated with decreasing opioid use, corresponding to 0.7 mg less per year older. The generalized linear model fitted for a gamma distribution included the following variables: ERAS *versus* PREHAB + ERAS, age, sex, and surgical approach. Older age and minimally invasive approach were associated with lower opioid use.

Although opioid use was lower in the PREHAB + ERAS group, the average maximum daily pain score was the same between the two groups (4.7 in the ERAS group *versus* 4.6 in the PREHAB + ERAS group, $P = 0.61$). Multivariable linear regression demonstrated that older age was associated with lower pain scores, whereas surgical approach, sex, and preoperative program (ERAS *versus* PREHAB + ERAS) were not. We also performed analyses on the postoperative inpatient daily use of nonopioid pain medications and found that there was no difference between the two groups in the use of acetaminophen, ketorolac, and gabapentin (Table 2). Multivariable linear regressions demonstrated no association of preoperative program or surgical approach with any of the medications; older age was associated with less use of ketorolac, and female sex was associated with less use of gabapentin.

A subgroup analysis of patients who activated their accounts to use the program demonstrated a difference of 15.9 mg between the ERAS and PREHAB + ERAS groups, representing a 29.9% decrease (53.0 mg *versus* 37.1 mg, $P = 0.036$). Subgroup analysis of the patients who signed up to participate but never activated their accounts and, thus, never used the program demonstrates no difference in the use of opioid pain medications after surgery (50.6 mg for ERAS *versus* 46.1 mg for PREHAB + ERAS, $P = 0.75$) (Fig. 2). The generalized linear model fitted for a gamma distribution for the use of opioids after surgery in the group that activated their accounts demonstrated that the PREHAB + ERAS program, older age, and minimally invasive surgery were significantly associated with less opioid use. Pain scores and the use of nonopioid pain medications did not differ between the ERAS and PREHAB + ERAS groups, regardless of whether they activated their online account or not (Table 3).

In the evaluation of whether there was an effect of time on postoperative opioid use, the generalized linear model (gamma distribution) of monthly averages of patients in the ERAS-only group (first and third time periods), which accounted also for age, sex, and surgical approach, demonstrated that the time variable was not significantly associated with the outcome. Older age, female sex, and open surgical approach were associated with higher levels of opioid use.

Another subgroup analysis of patients in the PREHAB + ERAS group was performed to determine if there was an association between engagement or adherence to the program and postoperative opioid use. We found that of the 157 patients who activated the online program by taking the baseline enrollment survey, 122 (77.7%) patients logged at least 1 day of physical activity or completed one of the weekly diet recall surveys. Of these patients, the average proportion of days that they filled out a physical activity survey to report their steps and strength exercises was 28.8%, and the average proportion of weeks that they filled out a weekly diet recall survey was 41%. Subjects walked more than 5000 daily steps on 62.6% of the logged days (19.4% of all program days) and did strength exercises on 76.8% of the logged days (24.3% of all program days). None of these factors were associated with postoperative opioid use. As part of the daily physical activity survey, those who did not reach their physical activity goal were asked why they were unable to do so. We found that higher frequency of stress as a cause for not achieving a physical activity goal was associated with higher levels of postoperative opioid use on bivariate analysis, but not in the generalized linear model adjusting also for age, sex, and surgical approach. Agreement with the statements “The walking program I did before surgery helped me recover” and “The strength exercises I did before surgery helped me recover” was associated with lower postoperative opioid use, adjusting for age, sex, and surgical approach in generalized linear models. This group of patients reported that they consumed at least five fruits/vegetables daily 60.7% of the time, at least two servings of fiber-rich foods daily 61.2% of the time, at least two servings of plant protein 56% of the time, foods with added sugar 31% of the time, and foods high in saturated fats 16.8% of the time. Diet behaviors were neither associated with postoperative opioid use, nor were in agreement with the statement “The changes I made to my diet before surgery helped me recover.”

Discussion

This observational cohort study examined the association of a web-based prehabilitation program and inpatient postoperative pain with opioid use after major abdominal colorectal surgery. We found that although pain scores were comparable between the patients who received the ERAS-only program and those who received the PREHAB + ERAS program, inpatient opioid use was 25% lower among those who received the PREHAB + ERAS program. The difference in opioid use between the two groups is unlikely to reflect a change in clinical practice over time, as part of the ERAS-only group underwent surgery in the months after the PREHAB + ERAS group. Older age and minimally invasive surgical approach were also associated with lower opioid use. The association between PREHAB + ERAS and lower opioid use was even more pronounced among participants who actually activated their accounts. The findings that the PREHAB + ERAS group had a 30% decrease in opioid use compared with the ERAS-only group among participants who activated their accounts to the web-based program, whereas there was no difference between the groups among those who did not activate their accounts, suggest that the difference in opioid use is linked to engagement with the prehabilitation component of the program. To contextualize this difference, patients in the PREHAB + ERAS group took the equivalent of about 10 mg of oxycodone less per inpatient postoperative day than patients in the ERAS-only group, who were taking the equivalent of 26 mg of oxycodone per day. This is a modest but clinically significant amount of opioids, albeit less of a difference than what one might see with the introduction of multimodal analgesics in the perioperative period (51 mg in OMEs for the first 24 h after surgery)[18] or with transversus abdominis plane block compared with placebo (23.7 mg in the first 24 h after surgery).[19]

The significance of this work is that it suggests that a preoperative nutrition and exercise program may be associated with lower postoperative opioid use, even without a reduction in pain perception. This phenomenon has not been explored in the surgical patient population, but there has been some evidence of reduced pain with exercise and improved dietary quality in a nonsurgical patient population.[12-15] Our finding that older patients have lower opioid requirements after major surgery is corroborated by previous work,[20,21] as are the findings of lower opioid requirements after minimally invasive surgery.

Our analysis of the degree of program engagement and adherence to the prehabilitation program within the PREHAB + ERAS group revealed that the frequency of program use and self-reported physical activity and dietary habits did not have an association with postoperative opioid use. However, believing that the preoperative walking and strength exercises helped them recovery was associated with lower opioid use.

The study has several limitations. The first is that this study design is subject to selection bias and time as a confounder. Patients who agreed to use an online platform that delivers a prehabilitation and perioperative information program may be more likely to use fewer opioids than those who agreed to use an online platform that only delivers perioperative information. As most of the patients in the ERAS-only group were enrolled during the first time period, it is possible that external influences, such as popular media coverage of the opioid epidemic, affected the way patients managed their pain after their operations. We did find that the time variable was insignificant, and there was no significant difference between the level of opioid use in the patients from the first and third time periods. The second limitation is that we only could include patients who had access to the internet and were agreeable and able to use a web-based program in English, which somewhat limits its generalizability. Another limitation of the study is that we did not measure the post-discharge use of opioid medications, so this analysis is based only on their inpatient use.

Conclusion

This study found that preoperative physical activity and nutrition optimization are associated with lower opioid use in the immediate postoperative period. Further research to explore the effects of preoperative exercise and nutrition on postoperative pain may be helpful in understanding this association. As this intervention was a highly scalable and economical way of deploying a prehabilitation intervention, such online programs can be incorporated into an overall strategy of reducing the risk of postoperative opioid dependence.

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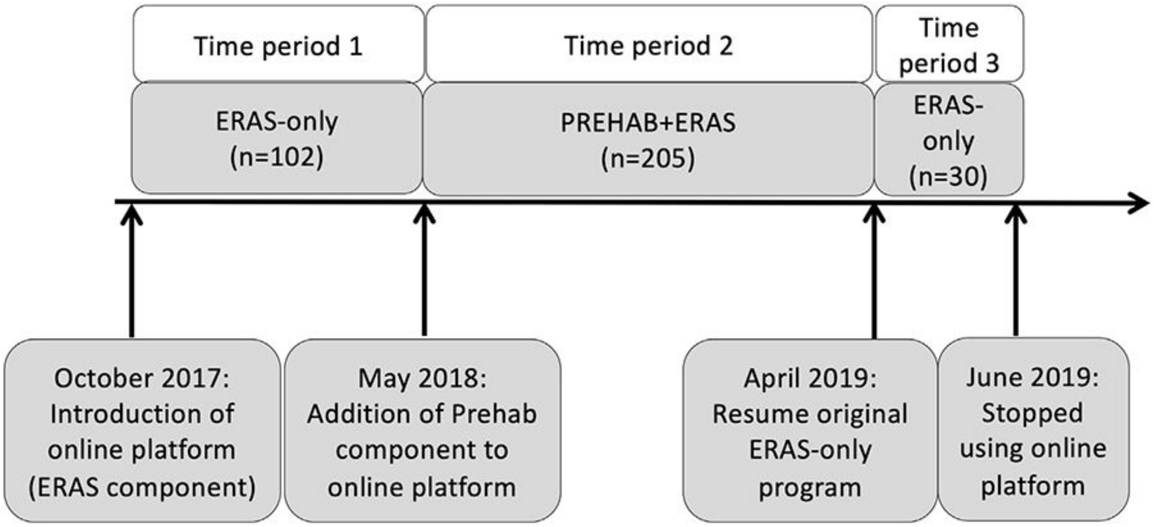

Fig. 1 –.
Patient cohorts over three consecutive time periods, with the ERAS-only program offered in the first and third time periods and the PREHAB + ERAS program offered in the second time period.

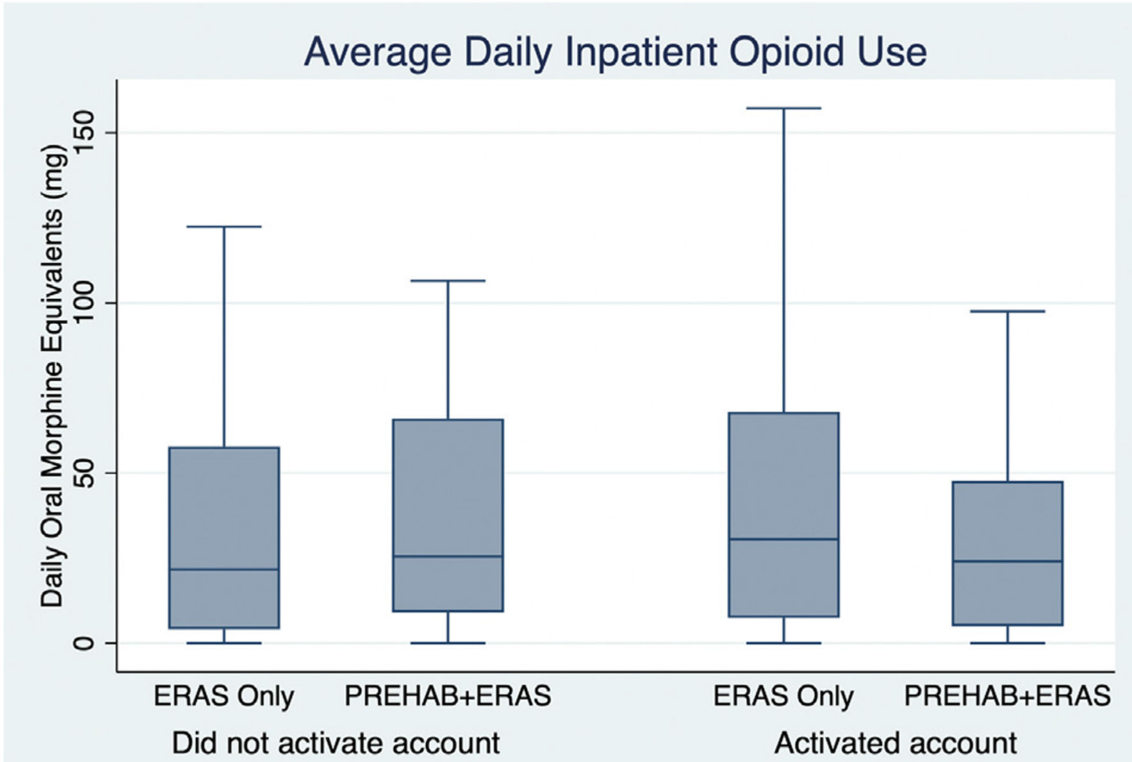

Fig. 2 –.

Patients who actually activated their accounts demonstrated a more pronounced difference in opioid use between the ERAS-only and PREHAB + ERAS groups.

Table 1 –

Demographic and operative characteristics.

Variable	Overall N = 337	ERAS n = 132	PREHAB + ERAS n = 205	P value
Sex				0.94
Male	47%	48%	47%	
Female	53%	52%	53%	
Mean age (SD)	56.5 (15.7)	57.9 (15.4)	55.7 (15.8)	0.19
Age group				0.91
18-44	22.6%	21.2%	23.4%	
45-54	21.1%	20.5%	21.5%	
55-64	23.7%	23.5%	23.9%	
65+	32.6%	34.9%	31.2%	
Body mass index (SD)	26.6 (6.2)	27.0 (6.4)	26.3 (6.02)	0.30
Surgical indication				0.11
Colorectal cancer	40.4%	32.6%	45.4%	
Diverticulitis	11.0%	11.4%	10.7%	
Ulcerative colitis	6.5%	5.3%	7.3%	
Crohn’s disease	9.8%	8.3%	10.7%	
Colostomy status	5.0%	6.8%	3.9%	
Ileostomy status	11.3%	13.6%	9.8%	
Rectal Prolapse	5.3%	6.8%	4.4%	
Other	10.7%	15.2%	7.8%	
Approach				0.07
Minimally invasive	56.8%	50.8%	60.7%	
Open	43.2%	49.2%	39.3%	
Median length of stay (IQR)	4 (2-5)	4 (3-6)	3 (2-5)	0.11

IQR = interquartile range; SD = standard deviation.

Table 2 –

Inpatient postoperative pain and pain medications, univariate analyses.

Variable	Overall $N = 337$	ERAS $n = 132$	PREHAB + ERAS $n = 205$	*P* value
Average max daily pain score (SD)	4.6	4.7	4.6	0.61
Average daily opioid dose, in oral morphine equivalents, in mg (SD)	44.3 (59.7)	52.3 (70.5)	39.2 (51.0)	0.049
Average daily acetaminophen dose, in mg (SD)	1849 (625)	1833 (628)	1860 (624)	0.70
Average daily ketorolac dose, in mg (SD)	13.1 (17.7)	12.3 (16.8)	13.6 (18.3)	0.91
Average daily gabapentin dose, in mg (SD)	606.7 (318.7)	598.1 (307.7)	610.6 (326.3)	0.73

SD = standard deviation.

Table 3 –

Pain and pain medication use, by account activation.

Variable	Activated account *n* = 250			Did not activate account *n* = 88		
	ERAS *n* = 92	**PREHAB + ERAS** *n* = 158	***P* value**	**ERAS** *n* = 40	**PREHAB + ERAS** *n* = 48	***P* value**
Average max daily pain score (SD)	4.7 (2.2)	4.4 (2.3)	0.26	4.7 (2.4)	5.3 (2.3)	0.27
Average daily opioid dose, in oral morphine equivalents, in mg (SD)	53.0 (68.1)	37.1 (49.8)	0.04	50.6 (76.6)	46.1 (55.0)	0.75
Average daily acetaminophen dose, in mg, (SD)	1856 (659)	1858 (670)	0.97	1780 (554)	1864 (445)	0.43
Average daily ketorolac, in mg (SD)	11.2 (16.8)	14.5 (18.6)	0.37	14.6 (16.8)	10.5 (17.2)	0.07
Average daily gabapentin, in mg (SD)	606 (321)	619 (344)	0.76	580 (277)	581 (261)	0.99

SD = standard deviation.