Observational Studies

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Long-term postoperative opioid prescription after cholecystectomy or gastric by-pass surgery: a retrospective observational study

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Abstract

Objectives: Opioids are commonly prescribed post-surgery. We investigated the proportion of patients who were prescribed any opioids 6–12 months after two common surgeries – laparoscopic cholecystectomy and gastric by-pass (GBP) surgery. A secondary aim was to examine risk factors prior to surgery associated with the prescription of any opioids after surgery.

Methods: We performed a retrospective observational study on data from medical records from patients who underwent cholecystectomy (n=297) or GBP (n=93) in 2018 in the Region of Västerbotten, Sweden. Data on prescriptions for opioids and other drugs were collected from the patients` medical records.

Results: There were 109 patients (28%) who were prescribed opioids after discharge from surgery but only 20 patients (5%) who still received opioid prescriptions 6–12 months after surgery. All 20 of these patients had also been prescribed opioids within three months before surgery, most commonly for back and joint pain. Only 1 out of 56 patients who were prescribed opioids preoperatively due to gallbladder pain still received prescriptions for opioids 6–12 months after surgery. Although opioid use in the early postoperative period was more common among patients who underwent cholecystectomy, the patients who underwent GBP were more prone to be "long-term" users of opioids. In the patients who were prescribed opioids within three months prior to surgery, 8 out of 13 patients who underwent GBP and 12 of the 96 patients who underwent cholecystectomy were still prescribed opioids 6–12 months after surgery (OR 11.2; 95% CI 3.1–39.9, p=0,0002). Affective disorders were common among "long-term" users of opioids and prior benzodiazepine and amitriptyline use were significantly associated with "long-term" opioid use.

Conclusions: The proportion of patients that used opioids 6–12 months after cholecystectomy or GBP was low. Patients with preoperative opioid-use experienced a significantly higher risk of "long-term" opioid use when undergoing GBP compared to cholecystectomy. The indication for being prescribed opioids in the "long-term" were mostly unrelated to surgery. No patient who was naïve to opioids prior surgery was prescribed opioids 6–12 months after surgery. Although opioids are commonly prescribed in the preoperative and in the early postoperative period to patients with gallbladder disease, there is a low risk that these prescriptions will lead to long-term opioid use. The reasons for being prescribed opioids in the long-term are often due to causes not related to surgery.

Keywords: cholecystectomy; diabetes; gastric by-pass; long-term opioids; opioid risk factors; postoperative opioid prescription.

Introduction

The use of opioids for pain management has increased dramatically during the last decades and an over-prescription of opioids in general has become a global health problem [1], especially in North America [2]. In a meta-analysis of 300,000 participants, a pooled incidence of opioid dependence or abuse of 5% among patients exposed to opioids was estimated [3]. In addition, side-effects are common; these include obstipation, confusion, drowsiness and most dangerously, opioid-induced central apnoea which can be fatal [4, 5].

Opioids are often used in the postoperative period and surgery is a common cause for the first opioid exposure [6]. For example, within seven days after certain types of low-

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risk surgery in the United States, 80% received opioids for post-operative pain [7]. Chronic postsurgical pain is defined as chronic pain that develops or increases in intensity after a surgical procedure and persists beyond the healing process, i.e., at least three months after the surgery [8]. In a recently published systematic review, it was stated that approximately 10% of patients still used opioids six month after surgery [9].

Some patients, e.g. patients with prior use of antidepressants and those previously prescribed habit-forming drugs are more prone to become chronic opioid users after elective surgery [10].

In Sweden, opioid over-prescription is considerably lower compared to North America [11, 12]. For example, the prescription of opioids within seven days after discharge for surgery procedures is 7-fold higher in North America compared to Sweden [11]. However, due to the potential risks of opioid misuse, it is important to for clinicians to gain knowledge about the extent of opioid use, especially in the long-term after surgery. Such information is also important for the individual patients.

The primary aim of this study was to examine the proportion of patients who were prescribed any opioids 6–12 months after two common surgeries – laparoscopic cholecystectomy and gastric by-pass (GBP) surgery, performed in the Region of Västerbotten, Sweden. The secondary aim was to examine factors associated with the prescription of opioids 6–12 months after surgery.

Materials and methods

Study design and data collection

This study is a retrospective observational study based on patients´ medical records from surgical clinics in the Region of Västerbotten, Sweden. In 2018, Västerbotten had approximately 270,000 inhabitants. To investigate opioids prescribed after surgery we focused on two operations – cholecystectomy and GBP surgery that are standardized and commonly performed in our region. Post-surgical abdominal pain is often reported after cholecystectomy [13] and after GBP surgery [14]. Cholecystectomy is mostly performed due to chronic disease (i.e. biliar colic or cholecystitis) [13] whereas GBP surgery is performed in patient without gastrointestinal disease. The surgeries were performed at hospitals in three Swedish cities (Umeå, Skellefteå and Lycksele). In the Region of Västerbotten all GBP surgeries are performed at Lycksele hospital and cholecystectomies are primarily performed at Skellefteå hospital. At Umeå University hospital cholecystectomy is performed only in special situations. The inclusion criterion for our study was having undergone cholecystectomy or GBP surgery in 2018. The patients were identified from the hospitals patient-registration-database by using ICD-10 codes for laparoscopic GBP (JDF11), other volume reduction of the ventricle (JDF96), other laparoscopic volume reduction of the ventricle (JDF97), cholecystectomy (JKA20), laparoscopic cholecystectomy (JKA21), other gallbladder operation (JKA96), and other laparoscopic gallbladder operation (JKA97). Patients who underwent gastric sleeve surgery (removal of 75–80% of the stomach) were included in the GBP group. Surgeries that had to be converted from laparoscopic to open surgery were included to examine differences in post-operative opioid use between these groups. All prescribed drugs by doctors (including general practitioners) in the catchment area are registered in the medical record system for Region Västerbotten. Information regarding prescriptions were collected from the list of prescribed drugs in the patient medical records and were registered as binary variables (yes/no). Postoperative opioid prescribed according to the medical records were registered from the date of surgery to one year after surgery. Being naïve to opioids was defined as not having any opioids prescribed three months before surgery.

Variables

Patients who underwent GBP surgery were compared with patients who were cholecystectomized for age, gender, BMI, smoking status, hospital, the diagnosis of diabetes, opioids and other drugs prescribed. Age was defined as the age at surgery. Body mass index (BMI) (kg/m^2) was based on measurements before surgery. Smoking status was defined as current smoker, previous smoker or never smoker. Diagnoses of diabetes (a known risk factor for neuropathy) were based on patient medical record notes and the continuous prescriptions of anti-diabetic drugs prior to surgery. Patients who were planned for open surgeries or were converted to open surgery were classified with the variable "open-surgery". Postoperative antibiotics were registered as an indication of a more complicated surgery. Three years prior to surgery, we registered if the patients at least once had been prescribed opioids, benzodiazepines (not used for insomnia), antidepressants, medications for insomnia, or medications for chronic pain (amitriptyline, gabapentin and pregabalin). In the postoperative period, we also measured the number of prescriptions a doctor had prescribed to the patients. The long-term treatment of opioids was defined as having at least one prescription of opioids in the period 6–12 months after surgery. For the patients who were prescribed opioids in the period 6–12 months after surgery, the cause for opioid treatment was more thoroughly checked in the medical records. In the opioid variables, in addition to strong opioids, other opioids such as codeine, tramadol and a combination of morphine, codeine, papaverine and noscapine (Spasmofen®) were included. Over the counter medications that patients could receive without prescriptions (i.e. paracetamol and NSAIDs) were not included.

Statistics

Student's *t*-tests were used for comparing age and BMI between patients who had cholecystectomy vs. those who had GBP. The Pearson's chi^2 test (or Fisher's Exact test when appropriate) was used to compare categorical data. The significance level was set at a p-value of 0.05. Odds ratios (OR) were described with 95th percent confidence intervals (CI). Potential preoperative risk factors for opioid prescriptions were registered and analysed with logistic regression with the dependent factor "any prescription of opioids" at three different time periods (within three months before surgery, within three months after surgery and in the period 6–12 months after surgery). In the logistic regression age (>50 years) and BMI (>30 kg/m^2) were used as binary

variables. Open surgery and converted from laparoscopic to open surgery were combined into one common variable in the logistic regression analysis. The hospital where the surgery was performed was also included as an independent variable. All patients who were prescribed opioids in the period 6–12 months after surgery were also prescribed opioids in the preoperative period. Therefore, in the logistic regression (Table 2, 6–12 months after surgery column) for the dependent variable "opioids within 3 years before surgery" we used a "dummy cell" to create an estimated adjusted OR. IBM SPSS version 26.0 was used for statistical analysis.

Results

Patient characteristics

There were 390 patients who underwent cholecystectomy (n=297) or GBP surgery (n=93) in 2018 that were included in the study. Table 1 presents baseline characteristics of the patients. None of the patients died or moved out of the region during the year after surgery. The surgeries were performed with a laparoscopic technique in all except 31 patients who had (or was converted to) an open cholecystectomy. In both groups, there were more women than men, and the proportion of women in the GBP group was significantly higher compared to the cholecystectomy group. The patients who underwent GBP were significantly younger and had significant higher BMI than those who underwent cholecystectomy. There were no significant differences in the prevalence of diabetes between the groups. There was a significantly higher use of antidepressants, amitriptyline and gabapentin/pregabalin for the GBP patients in the three-years before surgery compared to the cholecystectomy patients.

Smoking was excluded due to 42% of missing data, which made it impossible to analyse it as a risk factor.

Table 1: Descriptive data for patients who underwent cholecystectomy and gastric by-pass surgery in 2018 in the Region of Västerbotten, Sweden. Statistics: Chi^2 test and Student's *t* test were used to analyse group differences.

	Cholecystectomy (n=297)	Gastric by-pass (n=93	p-Value
Gender			
Men n, %	119 (40)	15 (16)	
Women n, %	178 (60)	78 (84)	**<0.001**
Age at surgery			
Mean age, years (SD)	52.5 (17)	40.9 (13)	**<0.001**
BMI at surgery, kg/m^2 (SD)	28.6 (4.9)	41.6 (6.5)	**<0.001**
Smoking status n, %			
Missing data	130 (44)	35 (38)	0.434
Current smoker	19 (6.4)	7 (7.5)	
Previous smoker	70 (24)	19 (20)	
Never smoker	78 (26)	32 (34)	
Hospital n, %			**<0.001**
Umeå	27 (9.1)	0 (0)	
Skellefteå	187 (63)	0 (0)	
Lycksele	83 (28)	93 (100)	
Planned open surgery n, %	13 (4.4)	0 (0)	**0.044**[a]
Prescribed any of the following medication within three months before surgery n, %			
Opioids	96 (33)	13 (14)	**0.001**
Benzodiazepines	10 (3)	1 (1)	0.471
Antidepressants	43 (14)	24 (26)	**0.010**
Medications for insomnia	58 (20)	21 (23)	0.555
Amitriptyline	8 (3)	7 (7)	0.057
Gabapentin or pregabalin	8 (3)	12 (13)	**<0.001**
Prescribed any of the following medication within three years before surgery n, %			
Opioids	143 (48)	40 (43)	0.386
Benzodiazepines	18 (6)	7 (8)	0.629
Antidepressants	67 (23)	34 (37)	**0.007**
Medications for insomnia	81 (27)	27 (29)	0.741
Amitriptyline	19 (6)	18 (20)	**<0.001**
Gabapentin or pregabalin	18 (6)	16 (17)	**0.001**

[a]Chi-Square, Fisher's Exact Test. **Bold P-values indicate significant associations**.

Opioids prescribed in the preoperative period

One-hundred-nine patients (28%) were prescribed opioids at least once three months before surgery. The proportion of patients who had preoperative opioid prescriptions were significantly higher for those who later underwent cholecystectomy compared to those who later underwent GBP (Table 1). However, in the three-year period before surgery, when patients receiving opioids only in the three months period before surgery were excluded, opioids were prescribed more often to the patients who later underwent GBP compared to those who later underwent cholecystectomy, but the difference was not significant (34 vs. 23%; p=0.075).

Opioids prescribed in the postoperative period

Figure 1 shows the number of times a patient was prescribed opioids in the year after surgery. Overall, 281 patients (72%) were not prescribed any opioids after being discharged from the surgery unit, 65 patients (17%) were only prescribed opioids once and 44 patients (11%) were prescribed opioids more than once. In the year after surgery, the number of prescriptions for opioids was higher in patients who underwent cholecystectomy compared to patients who underwent GBP (p=0.035) (Figure 1).

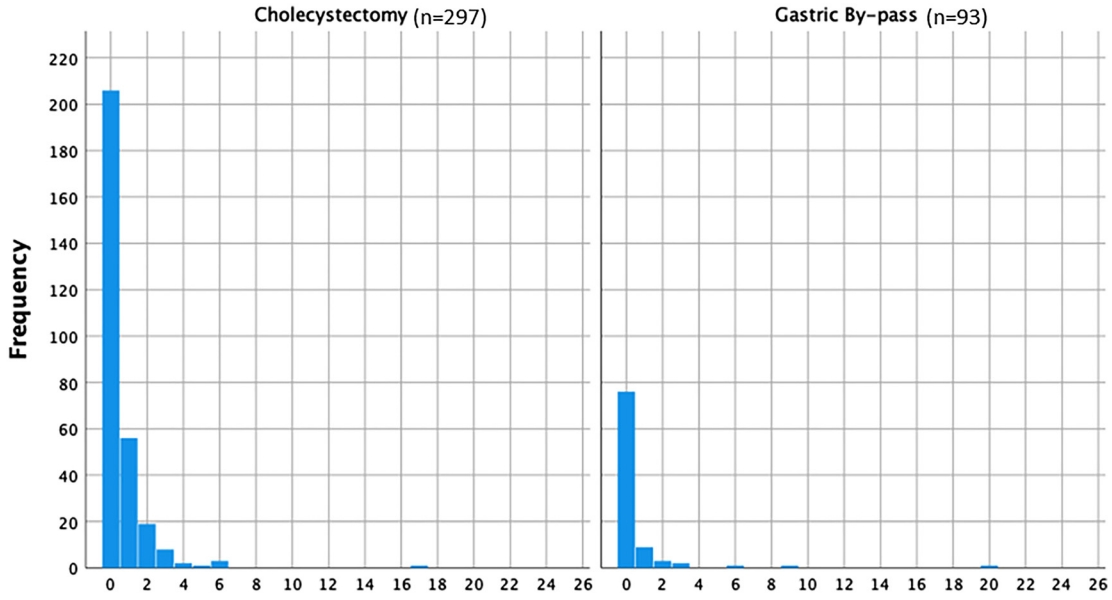

Figure 1: The number of prescriptions of opioids the year after cholecystectomy and gastric by-pass surgery (n=390).

In the early postoperative period (0–3 months), having cholecystectomy, age < 50 years, diabetes, open surgery, postoperative antibiotics and previous prescriptions for opioids were significantly associated with being prescribed opioids after discharge from the surgery unit (Table 2).

Patients who were prescribed opioids 6–12 months after surgery

Table 3 presents patients who were prescribed opioids 6–12 months after surgery and the association with pre-operative factors. Overall, only 20 patients (5.1%) were still prescribed opioids 6–12 months after surgery. Among 109 patients who were prescribed opioids after surgery 69% (75 patients) were naïve to opioids prior to surgery, but none of these patients was prescribed opioids 6–12 months after surgery.

In the patients who were prescribed opioids within three months prior to surgery, 8 out of 13 patients (62%) who underwent GBP and 12 of the 96 patients (12%) who underwent cholecystectomy were prescribed opioids > six months after surgery (OR 11.2; 95% CI 3.1–39.9: p=0.0002).

Figure 2 shows the number of times these 20 patients were prescribed opioids in the year after surgery. Twelve out of 20 patients were prescribed opioids 3 times or more. The opioids prescribed > six months after surgery were a combination of codeine and paracetamol (Citodon®) (eight patients), tramadol (six patients), oxycodone (three

Table 2: Logistic regression showing adjusted odds ratio for different independent variables impact on prescription of opioids before and after surgery. All patients (n=390) included.

	Any prescription of opioids		
	0–3 months before surgery (n=109)	**0–3 months after surgery (n=109)**	**6–12 months after surgery (n=20)**
Gastric by-pass[a]	**0.2 (0.08–0.5)**	**0.1 (0.05–0.3)**	3.1 (0.5–21)
Gender[b]	0.8 (0.4–1.3)	1.6 (0.9–3.1)	1.3 (0.4–4.3)
Age at surgery > 50 years	0.8 (0.5–1.4)	**0.5 (0.2–0.9)**	0.3 (0.07–1.2)
Body mass index > 30 kg/m^2	1.2 (0.7–2.1)	1.8 (0.9–3.5)	0.6 (0.1–2.5)
Diabetes	1.6 (0.7–3.8)	**3.4 (1.3–9.4)**	2.8 (0.5–16)
Hospital[c]	1.0 (0.5–1.7)	**0.2 (0.09–0.4)**	1.3 (0.3–6.3)
Open/converted[d]	0.6 (0.3–1.7)	**47 (13–173)**	3.0 (0.4–20)
Postoperative antibiotics	0.9 (0.4–2.0)	**3.9 (1.5–10)**	3.6 (0.6–20)
Prescriptions within three years before surgery			
Opioids (all types)	NA	**3.8 (2.1–6.9)**	**47 (2.7–828)**
Benzodiazepines	0.7 (0.3–1.9)	1.8 (0.7–4.8)	**4.9 (1.1–23)**
Antidepressants	1.1 (0.6–2.0)	1.6 (0.8–3.1)	1.8 (0.6–5.6)
Medications for insomnia	1.6 (0.9–3.0)	1.5 (0.7–3.0)	1.2 (0.4–4.1)
Amitriptyline	**2.4 (1.1–5.4)**	1.5 (0.6–3.8)	**6.1 (1.8–21)**
Gabapentin or pregabalin	1.5 (0.6–3.6)	1.1 (0.4–2.8)	0.8 (0.2–3.2)

NA, non-appropriate. [a]Cholecystectomy as reference. [b]Women as reference. [c]Lycksele Hospital as reference. [d]Planned open surgery or converted from laparoscopic to open surgery. **Bold values indicates significant associations**.

Table 3: The impact of surgery type, gender, age, BMI and preoperative medication use on postoperative opioid prescription 6–12 months after surgery. Chi^2 tests were used to analyse group differences.

	Prescription for opioids 6–12 months after surgery n, %	p-Values
Type of surgery		
Cholecystectomy (n=297)	12 (4.0)	
Gastric by-pass (n=93)	8 (8.6)	0.104
Gender		
Men (n=134)	6 (4.5)	
Women (n=256)	14 (5.5)	0.673
Age at surgery		
<50 years (n=200)	12 (6.0)	
>50 years (n=190)	8 (4.2)	0.423
Body mass index at surgery		
BMI < 30 (n=196)	8 (4.1)	
BMI > 30 (n=186)	12 (6.5)	0.299
Open/converted to open surgery		
Yes (n=31)	3 (9.7)	
No (n=359)	17 (4.7)	0.206
Hospital		
Umeå (n=27)	1 (3.7)	
Skellefteå (n=187)	8 (4.3)	
Lycksele (n=176)	11 (6.2)	0.655
Prescription within three months before surgery		
Opioids		
Yes (n=109)	20 (18)	
No (n=281)	0 (0)	**<0.001***
Benzodiazepines		
Yes (n=11)	3 (27)	**<0.015***
No (n=379)	17 (4.5)	
Antidepressants		
Yes (n=67)	5 (7.5)	0.361
No (n=323)	15 (4.7)	
Medication for insomnia		
Yes (n=70)	9 (11.4)	**0.009***
No (n=300)	11 (3.5)	
Amitriptyline		
Yes (n=15)	3 (20)	**0.036***
No (n=375)	17 (4.5)	
Gabapentin or pregabalin		
Yes (n=20)	3 (15)	0.075
No (n=370)	17 (4.6)	

***Bold values indicate significant associations.**

patients), ketobemidone (one patient) and a combination of morphine, codeine, papaverine and noscapine (Spasmofen®) (two patients).

The reason for being prescribed opioids 6–12 months after surgery was for the most part not associated with surgery. For example, 11 patients were prescribed opioids due to musculoskeletal pain, three patients due to chronic headache, one patient due to dysmenorrhea and one patient for an unknown cause. Only four patients were prescribed opioids due to abdominal pain and one of those patients received opioids due to postoperative pain related to a second surgery (volvulus) six months after a cholecystectomy. Five of the patients who were prescribed opioids > six months after surgery had diabetes (four patients due to musculoskeletal pain and one patient due to abdominal pain).

The reason for opioids being prescribed prior to surgery in these patients were mostly for reasons that were not directly related to overweight or gallbladder pain. Instead, most patients had opioids prescribed due to back, neck and joint pain (n=11), headache (n=3), neuropathic pain (n=3), pancreatitis (n=1) and residual pain from previous abdominal surgery (n=1). The most common opioid among these patients was the combination of codeine and paracetamol (Citodon®) (nine patients). The other prescriptions were tramadol (five prescriptions) and different types of stronger opioids (five prescriptions).

Interestingly, only one out of 56 patients who received the combination of morphine, codeine, papaverine and noscapine (Spasmofen®) prior to surgery for gallbladder related pain was still on opioids >six months after surgery.

Ten of the 20 patients (50%) who were prescribed opioids > six months after surgery were treated for affective disorders and five patients (25%) were treated for insomnia in the year after surgery. Six out of the 10 patients with affective disorders were also prescribed benzodiazepines

In the logistic regression analysis including all patients in the study, prior opioid, prior benzodiazepine and prior amitriptyline use were associated with any opioid prescription in the period 6–12 months after surgery (Table 2). When including only patients who were prescribed opioids in the preoperative period, having GBP, prior use of opioids, benzodiazepines and amitriptyline was associated with being prescribed opioids 6–12 months after surgery (Table 4).

Patients who underwent cholecystectomy

The indication for cholecystectomy was biliary colic (51%) cholecystitis (38%), gallstone pancreatitis (10%) and gallbladder polyps (1%). Ninety-two of the patients (31%) who underwent cholecystectomy were prescribed any opioids the year after surgery. The proportion of patients that were prescribed opioids post-surgery for different indications was biliary colic (35%), cholecystitis (27%) and gallstone pancreatitis (37%). There were no significant differences in opioid prescription post-surgery between the patients with different indications for cholecystectomy.

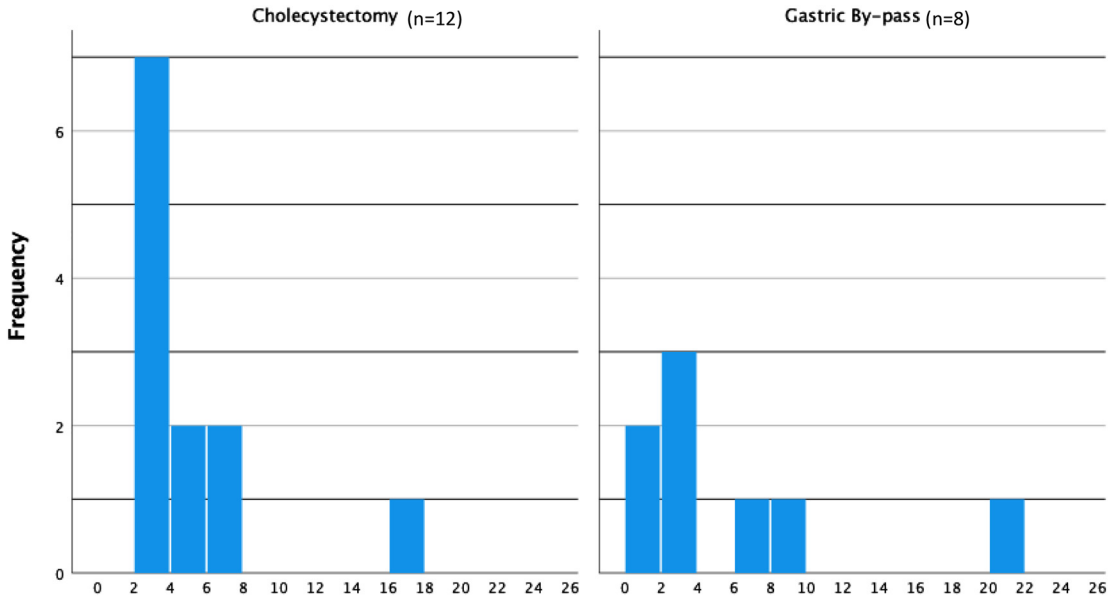

Figure 2: The number of prescriptions of opioids the year after cholecystectomy and gastric by-pass surgery in patients who were prescribed opioids six months after surgery (n=20).

Table 4: Logistic regression showing risk factors associated with being prescribed any opioids 6–12 months after cholecystectomy and gastric by-pass surgery. Only patients that were prescribed opioids three months prior to surgery are included (n=109).

	Univariate odds ratio (95% CI)	Multivariate odds ratio (95% CI)
Gastric by-pass[a]	**11.2 (3.1–40)**	**27 (1.9–372)**
Gender[b]	0.9 (0.3–2.7)	1.2 (0.2–5.5)
Age at surgery > 50 years	0.6 (0.2–1.6)	0.5 (0.1–2.8)
Body mass index > 30 kg/m^2	2.1 (0.8–5.7)	0.4 (0.1–3.1)
Diabetes	2.5 (0.7–9.4)	0.7 (0.1–7.7)
Hospital[c]	0.4 (0.2–1.1)	2.0 (0.3–12)
Open/converted[d]	3.0 (0.7–14)	3.4 (0.3–33)
Postoperative antibiotics	1.8 (0.4–7.4)	3.1 (0.4–26)
Prescriptions within three years before surgery		
Benzodiazepines	**9.6 (2.1–44)**	**25 (1.9–323)**
Antidepressants	**3.5 (1.3–9.5)**	1.9 (0.4–9.7)
Medications for insomnia	2.1 (0.8–5.5)	0.9 (0.2–5.1)
Amitriptyline	**11 (3.4–40)**	**9.5 (1.7–52)**
Gabapentin or pregabalin	2.5 (0.7–9.4)	1.2 (0.2–7.1)

[a]Cholecystectomy as reference. [b]Women as reference. [c]Lycksele Hospital as reference. [d]Planned open surgery or converted from laparoscopic to open surgery **Bold values indicates significant associations.**

Discussion

The primary aim of this retrospective observational study was to examine whether patients in our region undergoing common laparoscopic surgery were at risk to be prescribed opioids 6–12 months after surgery. Interestingly, there were only 20 patients (5%) who still received opioids 6–12 months postoperatively, and all of these patients were also prescribed opioids before surgery. Also, most patients who used opioids prior to surgery had stopped opioid use within six months after surgery (i.e. 89 out of 109 patients).

It was previously shown that prescriptions of opioids in Sweden is low compared to other countries. Ladha et al. [11] showed that the proportions of patients in Sweden in 2013–2014 who were prescribed opioids the first 7 days after four common surgeries (laparoscopic cholecystectomy, laparoscopic appendectomy, knee meniscectomy and breast excision) was low (approximately 11%) and was 7-fold lower than in North America. In the same study, it was shown that within the first 30 days after surgery, only 5% of the Swedish patients were prescribed more than 200 mg of morphine equivalents compared to 45% of the patients from United States.

In line with previous studies, our study showed that opioid use prior to surgery was a strong risk factor for long-term use after surgery [9]. However, the reasons for opioid use prior to surgery and post-surgery for the patients who were prescribed opioids 6–12 months after surgery were mostly back and joint pain, and the surgery *per se* or opioid treatment due to gall bladder disease was not the primary cause for receiving opioid prescriptions in the long-term. For example, only one out of 56 of the patients who received opioids due to gallstone attacks in the preoperatively received a prescription for opioids after six months.

As suspected and consistent with other studies [15, 16], we found that patients having open surgery (or was

converted to) was at a greater risk for receiving any opioid prescription after surgery. However, importantly in our study 28 out of the 31 patients who had had open surgery were no longer prescribed opioids > six months after surgery. This indicates that opioid use postoperatively after open cholecystectomy seems to be safe regarding the risk of long-term use of opioids.

Although opioid use in the early postoperative period was more common among patients who underwent cholecystectomy, the patients who underwent GBP were more prone to be "long-term" users of opioids than those who underwent cholecystectomy. For example, in patients who were prescribed opioids before surgery 86% of those who underwent cholecystectomy had stopped opioids after six months after surgery compared to only 38% of the patients with GBP. Preoperative musculoskeletal pain is common among patients admitted for GBP [17]. Obesity and chronic pain are comorbid conditions with a complex interplay involving several mechanisms [18]. Furthermore, obesity is a risk factor for chronic pain, and chronic pain is a risk factor for obesity [18]. Raebel et al. [19] studied the effect of chronic opioid use before and after bariatric surgery and found that 8% of the patients used opioids chronically before surgery and 77% of these patients continued to be chronic users of opioids after surgery. The authors also found that chronic opioid use was more common after than before surgery, and three years after surgery, 18% of the patients were chronic opioid users.

Previous studies have shown that anxiety/depression is a risk factor for opioid use [11] and for opioid use after surgery [9]. This complies with our study that showed that the prescription of benzodiazepines was a significant risk factor for being prescribed opioids 6–12 months after surgery. The use of antidepressants is common in patients with chronic pain, and approximately half of the patients treated with opioids for chronic non-cancer pain use antidepressants [20]. In our study, half of the patients who were prescribed opioids were treated for affective disorders in the year after surgery. However, when adjusted for other factors, the prescription of antidepressants was not significantly associated with long-term opioid use in our study.

We also found that prescriptions of amitriptyline were significantly associated with long-term opioid use. In Sweden, amitriptyline is mostly used for the treatment of neuropathic pain and the more frequent use of amitriptyline in the patients who were prescribed opioids 6–12 months in our study may reflect that these patients in general have a hypervigilance for pain signals.

One strength of our study was that in the Region of Västerbotten, there are no private surgery clinics that perform cholecystectomies or GBPs; therefore, the present study includes all patients who underwent cholecystectomies and GBP surgery in the region in 2018. Because of our medical record system, we were able to observe all patients one year after surgery and no patient had died or was lost to follow-up regarding opioid prescriptions. Furthermore, the medical computer record system in the Region of Västerbotten allows us to include all drug prescriptions of drugs except for some over-the-counter drugs (e.g. paracetamol and NSAIDs). There were also limitations in our study. The data regarding opioids and other drugs were thoroughly collected from the list of prescribed drugs in the patient medical records; however, we cannot be sure that the patients were actually taking their prescribed medicines. There was also difficulty in determining exactly the quantity of opioids prescribed using morphine milligram equivalents and we therefore decided to use a binary variable (prescription/no prescription) for opioid use.

Conclusion

Our study concludes that in our Region of Sweden, there is a low risk for "long-term" opioid use after laparoscopic cholecystectomy and GBP surgery. No patient who was naïve to opioids prior to surgery was prescribed opioids 6–12 months after surgery. There is no indication that preoperative use of opioids in patients with gallstone attacks will lead to "long-term" opioid use. Patients who underwent GBP were at risk for being prescribed opioids in the "long-term" but for indications unrelated to surgery.

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Competing interests: Authors state no conflict of interest.
Ethical approval: The study was classified as a non-interventional observations study and was approved by the Swedish Ethical Authority (Advisory board) (Dnr 2020-02443).

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