Long-term Analgesic Use After Low-Risk Surgery

A Retrospective Cohort Study

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Background: This study evaluated the risk of long-term analgesic use after low-risk surgery in older adults not previously prescribed analgesics.

Methods: We conducted a retrospective cohort study using linked, population-based administrative data in Ontario, Canada, from April 1, 1997, through December 31, 2008. We identified Ontario residents 66 years and older who were dispensed an opioid within 7 days of a short-stay surgery (cataract surgery, laparoscopic cholecystectomy, transurethral resection of the prostate, or varicose vein stripping) and assessed the risk of long-term opioid use, defined as a prescription for an opioid within 60 days of the 1-year anniversary of the surgery. In a secondary analysis, we examined the risk of long-term use of nonsteroidal anti-inflammatory drugs (NSAIDs). We used multivariate logistic regression to examine the association between postsurgical use of analgesics and long-term use.

Results: Among 391 139 opioid-naive patients undergoing short-stay surgery, opioids were newly prescribed to 27 636 patients (7.1%) within 7 days of being discharged from the hospital, and opioids were prescribed to 30 145 patients (7.7%) at 1 year from surgery. An increase in the use of oxycodone was found during this time (from 5.4% within 7 days to 15.9% at 1 year). In our primary analysis, patients receiving an opioid prescription within 7 days of surgery were 44% more likely to become long-term opioid users within 1 year compared with those who received no such prescription (adjusted odds ratio, 1.44; 95% CI, 1.39-1.50). In a secondary analysis, among 383 780 NSAID-naive patients undergoing short-stay surgery, NSAIDs were prescribed to 1169 patients (0.3%) within 7 days of discharge and to 30 080 patients (7.8%) at 1 year from surgery. Patients who began taking NSAIDs within 7 days of surgery were almost 4 times more likely to become long-term NSAID users compared with patients with no such prescription (adjusted odds ratio, 3.74; 95% CI, 3.27-4.28).

Conclusion: Prescription of analgesics immediately after ambulatory surgery occurs frequently in older adults and is associated with long-term use.

Arch Intern Med. 2012;172(5):425-430

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PATIENTS ARE OFTEN PRESCRIBED analgesics after ambulatory and short-stay operations preemptively in anticipation of postoperative pain.[1] In many cases, patients are given a standard dose based on the expectation of postoperative pain.[2] Indeed, recent evidence has shown that overprescription of narcotics is common, and retained surplus medication presents a readily available source of opioid diversion among certain surgical patients.[3]

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The most common analgesics prescribed to outpatients are opioids and nonsteroidal anti-inflammatory drugs (NSAIDs).[1] Although opioids can be beneficial, they are also commonly associated with adverse events, such as sedation, constipation, and respiratory depression.[4,5] Their long-term use can lead to physiologic tolerance and addiction. NSAIDs are associated with adverse gastrointestinal events, including ulcers, renal dysfunction, and hypertension.[4-6] Although postsurgical analgesic treatment is often intended for short-term use, their administration may lead to regular longer-term use, thereby placing the patient at increased risk for drug-related harm.

We sought to determine whether de novo administration of analgesics to elderly patients after short-stay operations was associated with long-term use of these medications. We focused on elderly persons because of the greater risk of adverse reactions to pain medicines in this group.

METHODS

We conducted a retrospective, nested-cohort study among a population of 1.4 million residents of Ontario, Canada, who were 66 years

and older. Two separate cohorts were constructed to examine the 2 analgesic patient groups: opioid and NSAID users. We used multiple health administrative databases in Ontario to identify patients 66 years and older who underwent short-stay operations from April 1, 1997, through December 31, 2008. Prescription medications were identified using the Ontario Drug Benefit database, which records data on all prescription medications dispensed to patients older than 65 years.[7] The Canadian Institute for Health Information Discharge Abstract Database was used to obtain information on all hospitalizations in Ontario, and inpatient and outpatient physician services were identified using the Ontario Health Insurance Plan physician-billing database.[8,9] The Registered Persons Database contains demographic and vital status information for each Ontario resident, and cancer diagnoses were obtained from the Ontario Cancer Registry, which contains information on patients in Ontario who are diagnosed as having cancer.[10] These databases were linked in an anonymous manner using unique encrypted health card numbers at the Institute for Clinical Evaluative Sciences in Toronto and are used frequently to study population-based health outcomes.[11-13]

Individuals 66 years and older who were discharged alive after low-pain short-stay surgery hospitalizations in Ontario during the study period were included in each cohort. Low-pain operations were defined based on clinical experience as operations primarily ambulatory in nature that are not generally associated with high levels of postoperative pain. The following operations were included: (1) cataract surgery, (2) laparoscopic cholecystectomy, (3) transurethral resection of the prostate, and (4) varicose vein stripping surgery. The index date was defined as the date of hospital discharge.

We excluded all patients who received at least 1 prescription for the cohort-specific analgesic (either opioids or NSAIDs) in the year before hospital admission and those who died in the 425 days of follow-up after hospital discharge. We also excluded patients who were admitted to the hospital for longer than 3 days to exclude patients who may have experienced significant complications related to their surgery. Individuals hospitalized in the 100 days before the index date were excluded from the analysis to ensure that any new analgesic prescription could be attributed to the surgery. Furthermore, we excluded operations conducted on an emergency basis and patients who had received any palliative care services or who were diagnosed as having cancer in the year before their surgery or within the 425-day follow-up period. These criteria were applied to more confidently ascribe the long-term analgesic prescription to the short-stay surgery and to minimize confounding related to other indications. For individuals who underwent more than 1 procedure that met the eligibility criteria during the study period, we only included the first such surgical procedure.

In the primary analysis, we defined exposure as administration of any opioid prescription within 7 days of hospital discharge. Patients were followed up thereafter for a maximum of 425 days to identify long-term opioid use. Long-term opioid use was defined as an additional claim for any opioid within 60 days of the 1-year anniversary date (eg, 305-425 days after the index date). In a secondary analysis, we replicated this study to investigate the association between postsurgical NSAID treatment initiation and long-term NSAID use.

We examined baseline characteristics of eligible patients in each analgesic medication cohort, stratified by exposure status, and standardized differences were used to test for differences between groups. A standardized difference of more than 0.10 is generally considered to indicate a meaningful difference.[14] We used multivariate logistic regression to examine the association between analgesic initiation after short-stay surgery and long-term analgesic use. We adjusted for potential confounding factors, including age, sex, Charlson comorbidity index, socioeconomic status (neighborhood income quintile based on census data), residence in a long-term care facility, and hospital type (teaching hospital or community hospital). All reported *P* values were 2-tailed and used a type 1 error rate of .05 as the threshold for statistical significance. Analyses were conducted using SAS statistical software, version 9.2 (SAS Institute Inc). The study was approved by the Research Ethics Board of Sunnybrook Health Sciences Centre, Toronto, Ontario.

RESULTS

OPIOID TREATMENT

During the study period, 391 139 patients who were opioid naive and met our inclusion criteria underwent short-stay surgery. Of these, 27 636 (7.1%) were issued a prescription for an opioid within 7 days of the index date; by surgical indication, 18 231 of 371 438 persons (4.9%) were prescribed opioids for cataract surgery; 7151 of 10 944 persons (65.3%) were prescribed opioids for laparoscopic cholecystectomy, 1211 of 6705 persons (18.1%) were prescribed opioids for transurethral resection of the prostate, and 1043 of 2052 persons (50.8%) were prescribed opioids for varicose vein stripping surgery. A total of 30 145 patients (7.7%) were prescribed opioids at 1 year from surgery. Patients who received early treatment with opioids were almost 2 years younger but had similar Charlson comorbidity scores and socioeconomic status compared with non–early users (**Table 1**). A total of 2857 (10.3%) of these patients were identified as long-term opioid users 1 year after surgery. A total of 27 288 of the 363 503 patients (7.5%) were not prescribed an opioid within 7 days of surgery and received an opioid prescription within 60 days of the 1 year anniversary after surgery. After multivariate adjustment, patients receiving an opioid prescription within 7 days of surgery were approximately 44% more likely than those who received no prescription to become long-term opioid users (adjusted odds ratio, 1.44; 95% CI, 1.39-1.50) (**Table 2**).

Among all patients receiving an early prescription for opioids, the most commonly prescribed opioid was codeine (93.4%; **Table 3**). Oxycodone was the second most frequently prescribed opioid (5.4%). Codeine remained the most commonly used opioid at 1 year after surgery (87.5%), but long-term opioid users also used more potent long-acting opioids, including transdermal fentanyl (1.6%) and oxycodone (15.9%).

Among the early users group, those who received a prescription within 60 days of the 1-year anniversary after surgery had more prescriptions than those who did not (mean number of prescriptions, 3.1 vs 1.3; $P < .001$). Similarly, the total supply of medication in the year after hospital discharge was higher (mean days of medication supplied, 33.3 vs 7.5; $P < .001$).

NSAID TREATMENT

In our secondary analysis, 383 780 patients were hospitalized for a short-stay surgery and met our inclusion criteria. Of these, 1169 (0.3%) were early NSAID users (prescribed NSAIDs within 7 days of index date) and were approximately 1½ years younger than non-NSAID

Table 1. Baseline Characteristics of Patients[a]

Characteristic	Opioid Cohort			NSAID Cohort		
	Non–Early Opioid Users (n = 363 503)	Early Opioid Users (n = 27 636)	Standardized Difference	Non–Early NSAID Users (n = 382 611)	Early NSAID Users (n = 1169)	Standardized Difference
Age, y						
Mean (SD)	76.81 (6.23)	75.31 (6.31)	0.24	76.76 (6.30)	75.22 (6.08)	0.24
Median (IQR)	77 (72-81)	75 (70-80)	0.24	77 (72-81)	75 (70-80)	0.24
Male sex	137 495 (37.8)	10 733 (38.8)	0.02	148 142 (38.7)	470 (40.2)	0.03
Charlson comorbidity index						
0	159 189 (43.8)	10 060 (36.4)	0.15	166 601 (43.5)	512 (43.8)	0.01
1	31 268 (8.6)	2262 (8.2)	0.01	35 793 (9.4)	107 (9.2)	0.01
2	19 445 (5.3)	1345 (4.9)	0.02	22 983 (6.0)	58 (5.0)	0.04
≥3	12 663 (3.5)	831 (3.0)	0.03	16 718 (4.4)	38 (3.3)	0.05
No hospitalization	140 938 (38.8)	13 138 (47.5)	0.18	140 516 (36.7)	454 (38.8)	0.04
SES quintile						
First (lowest)	73 837 (20.3)	5620 (20.3)	0	78 497 (20.5)	233 (19.9)	0.01
Second	78 188 (21.5)	6032 (21.8)	0.01	82 445 (21.5)	244 (20.9)	0.02
Third	72 690 (20.0)	5334 (19.3)	0.02	75 760 (19.8)	248 (21.2)	0.04
Fourth	67 789 (18.6)	5048 (18.3)	0.01	71 036 (18.6)	210 (18.0)	0.02
Fifth (highest)	70 032 (19.3)	5537 (20.0)	0.02	73 814 (19.3)	231 (19.8)	0.01
Unknown	967 (0.3)	65 (0.2)	0.01	1059 (0.3)	≤5	0
Residence in an LTC facility	4818 (1.3)	306 (1.1)	0.02	5836 (1.5)	12 (1.0)	0.04
Residence in LTC unknown	9802 (2.7)	1005 (3.6)	0.06	10 684 (2.8)	30 (2.6)	0.01
Teaching hospital	86 677 (23.8)	6737 (24.4)	0.01	93 334 (24.4)	258 (22.1)	0.05

Abbreviations: LTC, long-term care; IQR, interquartile range; NSAID, nonsteroidal anti-inflammatory drug; SES, socioeconomic status.
[a]Data are presented as number (percentage) of patients unless otherwise indicated.

Table 2. Risk of Long-term Analgesic Use After Low-Risk, Short-Stay Surgery

Primary Outcome	Opioid Cohort			NSAID Cohort		
	No. of Events in Non–Early Users	No. of Events in Early Users	Adjusted Odds Ratio (95% CI)	No. of Events in Non–Early Users	No. of Events in Early Users	Adjusted Odds Ratio (95% CI)
All operations	27 288	2857	1.44 (1.39-1.50)	29 795	285	3.74 (3.27-4.28)
Cataract surgery	26 584	2102	1.62 (1.54-1.67)	28 093	247	4.61 (3.98-5.35)
Laparoscopic cholecystectomy	222	549	1.33 (1.13-1.56)	1089	15	1.14 (0.67-1.96)
Transurethral resection of the prostate	425	123	1.33 (1.07-1.64)	440	17	4.10 (2.36-7.14)
Varicose vein stripping	57	83	1.41 (0.99-2.02)	173	6	0.82 (0.35-1.95)

Abbreviation: NSAID, nonsteroidal anti-inflammatory drug.

users (Table 1). A total of 30 080 patients (7.8%) were prescribed NSAIDs at 1 year after surgery. These patients also had similar Charlson comorbidity scores and socioeconomic status as those who were not prescribed early NSAIDs. Furthermore, 285 of these patients (24.4%) continued to receive long-term NSAID therapy 1 year after surgery. Approximately, 29 795 of the 382 611 patients (7.8%) who were not prescribed an NSAID within 7 days of surgery received long-term NSAID therapy. In a multivariate logistic regression analysis, patients receiving an early NSAID prescription were 3.7 times more likely to become long-term NSAID users compared with those who did not receive an NSAID prescription within 7 days (adjusted odds ratio, 3.74; 95% CI, 3.27-4.28; Table 2).

Among the early users group, those who received a prescription within 60 days of the 1 year anniversary after surgery had more prescriptions than those who did not (mean number of prescriptions, 6.1 vs 1.8; $P<.001$). Similarly, the total supply of medication in the year after hospital discharge was higher (190 vs 46 days, $P<.001$).

COMMENT

We found that approximately 7% of patients are prescribed opioids within 7 days after a low-pain surgery and more than 10% of them continued to use these medications 1 year later. Similarly, approximately one-quarter of patients prescribed NSAIDs postoperatively after a low-pain surgery continued to use these medications after 1 year of follow-up. More important, many individuals initially prescribed low-potency opioids had transitioned to more potent opioids, such as oxycodone, within 1 year of the surgery.

Our observation that early postoperative analgesic prescription is associated with long-term use is novel but

Table 3. Distribution of Opioid Prescribing Among Patients Newly Dispensed an Opioid Within 7 Days After Surgery and at 1-Year Follow-up

Opioid Name	Frequency Prescribed, %[a]	
	First 7 Days After Surgery	1-Year Follow-up
Codeine	93.4	87.5
Fentanyl patch	0.01	1.6
Hydromorphone	0.3	1.9
Meperidine	0.7	1.0
Morphine	0.1	2.6
Oxycodone	5.4	15.9
Long-acting oxycodone	0.04	1.9

[a]Calculated among people receiving at least 1 opioid prescription. If someone received multiple opioid types, they were counted multiple times.

has been seen with other medications with misuse potential in seniors during the perihospitalization period.[15] Most studies suggest that pain is poorly managed in the postoperative period, and more liberal use of analgesics is advocated.[1] Although the use of these medications is likely justified for operations in which postoperative pain is a major concern, little is known about patterns of analgesic use in operations in which postoperative pain is usually not a significant consideration. This may be particularly worrisome when patients are prescribed standardized doses of analgesics to take at their discretion, regardless of the anticipated severity of postoperative pain.

It is concerning that more than 10% of those initially prescribed opioids and almost 25% of those initially prescribed NSAIDs are also prescribed the medications 1 year after the surgery. This high prevalence is compounded by the consideration that our study focused solely on operations that are not generally associated with long-term postoperative pain, with the possible exception of some individuals who underwent laparoscopic cholecystectomy. If we considered other operations and other analgesic prescriptions, the number of individuals at risk for long-term analgesic use would almost certainly be higher. Indeed, the population-based nature of the study and the general practice of postoperative prescriptions address some of the widespread generalizability of our findings beyond the setting and types of operations.

The types of analgesics prescribed both early and afterward may also affect elders postoperatively. Despite codeine possessing unpredictable pharmacokinetics and analgesic properties, we found it to be the most commonly prescribed opioid in both the short and long terms.[16-18] This finding is concerning because recent work has suggested an association between long-term codeine use and risk of injury and adverse cardiovascular events among seniors.[19,20] Our findings suggest that the prescription of codeine after short-stay surgery may contribute to the use of other potent opioids, such as oxycodone, which have been shown to be associated with increased morbidity and mortality.[20,21] These points do not even consider that the continued use of opioids after 1 year raises the possibility that the exposure may result in addiction or physical dependence.[4]

Several limitations of our study merit emphasis. Mainly, we do not know why analgesics were prescribed in both the early and late postoperative phases of our study. It is possible that we captured individuals who initiated use of an opioid postoperatively for a poorly managed, preexisting pain condition. Thus, our definition of long-term use among these individuals could mean that, with the initiation of analgesics, these patients had a significant improvement in symptoms with continued use. In this manner, the initiation of analgesic therapy both postoperatively and in the long term may have been entirely suitable for a subset of patients examined. However, this is unlikely because of our cohort inclusion requirement of at least 1 year free from any opioid prescriptions. This requirement also helps to address additional confounding related to unmeasured patient differences in disposition to use of analgesics other than just the exposure to the initial prescription. Although no analysis of observational data can eliminate confounding, we believe that our methods have minimized some of its effects.

Similarly, we acknowledge that individuals who have acute pain in the postoperative period, regardless of the type of surgery, may have a higher likelihood of having associated chronic pain and may therefore use analgesics in the long term. Indeed, sometimes acute postsurgical pain is linked with individuals developing chronic pain.[22,23] Specifically, laparoscopic cholecystectomy has been associated with chronic postsurgical pain in several studies, albeit in only a few patients.[22,24,25] However, if chronic pain is the only substantive factor governing long-term opioid or NSAID use in patients undergoing laparoscopic cholecystectomy, we would expect the risk of long-term opioid use to be higher for this surgery compared with the other groups. In fact, the point estimate for the laparoscopic cholecystectomy group was lower than the overall mean for the entire cohort. Furthermore, the risk of long-term NSAID use among individuals who underwent laparoscopic cholecystectomy was relatively small. Thus, we believe there must be other reasons that explain this long-term opioid and NSAID use postoperatively.

The analyses may also underestimate the true postoperative analgesic exposure rate for prescriptions related to the surgery but dispensed 8 days or more after hospital discharge. However, we believe this would represent a small proportion of individuals because most with acute pain after surgery would fill prescriptions within 7 days of discharge. Similarly, by excluding patients who died within 425 days of hospital discharge, we may have underestimated the strength of our association because these deaths may have been related to opioid- or NSAID-related adverse events. Furthermore, the data could not capture those individuals who were already using over-the-counter NSAIDs preoperatively. However, we believe that this would have represented a relatively small fraction of individuals and would not have substantially changed the results.

Long-term postoperative analgesic use may best be addressed by preventing its initiation. Further research

will be required to determine the exact mechanisms behind the continued use of postoperative opioids and NSAIDs among elderly populations before a suitable solution can be customized. Yet, interventions such as the development of electronic medical records and medication reconciliation programs or models of care that facilitate communication and coordination between perioperative and community-based physicians may help further reduce the risk of progression from short-term to long-term analgesic use.[26-30] Furthermore, initiatives that tailor postoperative analgesic prescriptions to patients after short-stay surgery could also help prevent this phenomenon. Larger-scale administrative policies, such as tighter regulations regarding the prescription of opioids after ambulatory surgery, may be successful in curtailing the long-term prescription of opioids postoperatively. Regardless, more research will be required to see whether any of these measures can provide a sustained effect.

As rates of ambulatory surgery among elderly populations increase, preventing analgesic therapy initiation could have far-reaching implications for those involved in the perioperative care of this population.[31] Concerted patient safety efforts must continue to focus on providing an opportunity for patients to heal from operations free of short-term pain while minimizing the risks of long-term adverse events.

Accepted for Publication: December 4, 2011.
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Author Contributions: *Study concept and design:* Alam, Gomes, Mamdani, Juurlink, and Bell. *Acquisition of data:* Alam, Zheng, and Bell. *Analysis and interpretation of data:* Alam, Gomes, Mamdani, Juurlink, and Bell. *Drafting of the manuscript:* Alam, Zheng, and Bell. *Critical revision of the manuscript for important intellectual content:* Alam, Gomes, Mamdani, Juurlink, and Bell. *Statistical analysis:* Alam, Zheng, Mamdani, Juurlink, and Bell. *Obtained funding:* Alam, Juurlink, and Bell. *Administrative, technical, and material support:* Alam and Mamdani. *Study supervision:* Juurlink and Bell.
Financial Disclosure: Dr Mamdani reported having served on advisory boards for the following companies: Hoffman La Roche, GlaxoSmithKline, Pfizer, Novartis, Eli Lilly and Company, Novo Nordisk, Astra Zeneca, and Bristol-Myers Squibb.
Funding/Support: This study was supported by the Institute for Clinical Evaluative Sciences, which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care. Dr Bell is supported by a Canadian Institutes of Health Research and Canadian Patient Safety Institute chair in Patient Safety and Continuity of Care. The Ontario Drug Policy Research Network/Ministry of Health and Long-Term Care fully funded this project.
Role of Sponsors: These funding agencies had no role in the design and conduct of the study; collection, management, analysis, or interpretation of the data; or preparation, review, or approval of the manuscript.
Disclaimer: The opinions, results, and conclusions reported in this article are those of the authors and are independent from the funding sources. No endorsement by the Institute for Clinical Evaluative Sciences or the Ontario Ministry of Health and Long-Term Care is intended or should be inferred.

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EDITOR'S NOTE

Harm From Long-term Opioid Therapy

As part of our "Less Is More" series, the *Archives* has recently published several articles on the dangers of opioid use for chronic pain. In this issue of the *Archives*, we publish a commentary on how women may be more vulnerable to harm from long-term opioid therapy than men.[1] Although all drugs have adverse effects, we are concerned about the use of opioids for chronic pain because of the lack of efficacy data for pain lasting longer than 16 weeks; the widespread use of opioids; the number of serious adverse effects, including death, attributable to opioid use; and the open question, addressed in a commentary in this issue of the *Archives*, as to what we are treating when we use opioids for chronic noncancer pain.[2] We thought that this article was a good reminder that initiation of short-term opioid therapy may lead to their longer-term use. We should be certain with any drug we prescribe that the benefits justify the risk. In the case of this study, it is unclear why 7% of elderly persons who were not previously taking opioids should have required them for minor operations known to cause little pain or why 8% of those who received an opioid for acute pain associated with minor surgery were still taking opioids 1 year later. We believe that when it comes to opioid administration for minor surgery, among older persons, less is more.

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Images From Our Readers

Dusk sky clouds, Berwyn, Pennsylvania.

Courtesy of: Humberto Guerra-Garcia, MD, MPH, Community Plan of Delaware, UnitedHealthcare, Berwyn, Pennsylvania.