Opioid Use Disorder is Associated With Complications and Increased Length of Stay After Major Abdominal Surgery

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Objective: The objective of this study was to determine the impact of opioid use disorder (OUD) on perioperative outcomes after major upper abdominal surgeries.

Summary of Background Data: OUD, defined as dependence/abuse, is a national health epidemic. Its impact on outcomes after major abdominal surgery has not been well characterized.

Methods: Patients who underwent elective esophagectomy, total/partial gastrectomy, major hepatectomy, and pancreatectomy were identified using the National Inpatient Sample (2003–2015). Propensity score matching by baseline characteristics was performed for patients with and without OUD. Outcomes measured were in-hospital complications, mortality, length of stay (LOS), and discharge disposition.

Results: Of 376,467 patients, 1096 (0.3%) had OUD. Patients with OUD were younger (mean 53 vs 61 years, $P < 0.001$) and more often male (55.1% vs 53.2%, $P < 0.001$), black (15.0% vs 7.6%, $P < 0.001$), Medicaid beneficiaries (22.0% vs 6.4%, $P < 0.001$), and in the lowest income quartile (32.6% vs 21.3%, $P < 0.001$). They also had a higher rate of alcohol (17.2% vs 2.8%, $P < 0.001$) and nonopioid drug (2.2% vs 0.2%, $P = 0.023$) dependence/abuse. After matching (N = 1077 OUD, N = 2164 no OUD), OUD was associated with a higher complication rate (52.9% vs 37.3%, $P < 0.001$), including increased pain [odds ratio (OR) 3.5, $P < 0.001$], delirium (OR 3.0, $P = 0.004$), and pulmonary complications (OR 2.0, $P = 0.006$). Additionally, OUD was associated with increased LOS (mean 12.4 vs 10.6 days, $P = 0.015$) and nonroutine discharge (OR 1.6, $P < 0.001$). In-hospital mortality did not differ (OR 2.4, $P = 0.10$).

Conclusion: Patients with OUD more frequently experienced complications and increased LOS. Close postoperative monitoring may mitigate adverse outcomes.

Keywords: esophagectomy, gastrectomy, hepatectomy, opioid use disorder, pancreatectomy, perioperative complications

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Opioid use disorder (OUD), defined as opioid dependence or abuse according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition,[1] has become a national health epidemic. In the United States, an estimated 2 million individuals have prescription-related OUD, which has also been associated with an increase in illicit opioid use, such as heroin and fentanyl.[2] Since 2001, opioid-related mortality, driven largely by illicit opioid overdose, has increased more than 5-fold, with 47,600 deaths reported in 2017 alone.[3,4] Surgery ranks second highest in opioid prescription rates, and the incidence of new persistent narcotic use can reach 6.5% among opioid-naïve postoperative patients.[5,6] The potential role of healthcare providers in the opioid epidemic has spurred increased scrutiny of perioperative opioid use,[7] but the care of surgical patients with a pre-existing history of OUD remains a challenge.

The impact of chronic opioid use and OUD on perioperative outcomes has been best described in orthopedic and spine surgery. Preoperative prescription opioid use in these settings has been associated with increased opioid demand perioperatively and decreased opioid independence on long-term follow-up.[8–11] In some cases, increased perioperative morbidity, hospital length of stay (LOS), readmissions, and resource utilization have also been identified.[9–11] Patients with a history of OUD, and not just chronic use, may also experience increased risk of perioperative mortality after elective orthopedic surgery.[12] After cardiovascular surgery, OUD has similarly been associated with increased in-hospital complications, LOS, cost, and nonroutine discharge disposition.[13]

The impact of OUD on outcomes in major abdominal operations has been less well characterized. Several studies have investigated postoperative outcomes in abdominopelvic surgical patients with a history of preoperative prescription opioid exposure.[14,15] However, not all patients with a history of narcotic use necessarily have opioid dependence or abuse, and, in those with OUD, opioid sources often include nonmedical and illicit avenues.[16,17] With the rising prevalence of nonmedical prescription or illicit OUD in the general population,[16–18] healthcare providers are increasingly caring for patients with this disorder in the perioperative setting. Therefore, it is important to characterize the specific impact of OUD on outcomes after high-risk abdominal operations.

We sought to determine the effect of OUD on perioperative outcomes in patients who underwent elective major upper gastrointestinal and hepatopancreatobiliary surgery, including esophagectomy, partial and total gastrectomy, major hepatectomy, and pancreatectomy. The outcomes measured included in-hospital complications, mortality, LOS, and discharge disposition. We hypothesized that a history of OUD is independently associated with not only increased postoperative pain and difficulty with pain control, but also other perioperative complications and disposition challenges after high-risk, abdominal operations.

METHODS

Data Source

A retrospective population-based study was performed using the 2003–2015 data from the Healthcare Cost and Utilization Project National Inpatient Sample (NIS), a hospital administrative database managed by the Agency for Healthcare Research and Quality.[19] The NIS is the largest all-payer inpatient healthcare database in the

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United States and represents more than 97% of the population. Using provided weights, it allows for national estimates of hospitalizations and treatments. All data are compliant with the Health Insurance Portability and Accountability Act. Because of the retrospective nature of the study and inability to identify individual patients or hospitals, institutional review board approval was not required.

Patient Selection

The NIS captures 30 diagnoses and 15 procedures per admission that are classified using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. Patients 18 years of age or older who had a primary procedure code of elective esophagectomy (42.40–2), gastrectomy (43.5–8, 43.91, 43.99), hepatectomy (50.22, 50.3), and pancreatectomy (52.51–3, 52.59, 52.6–7) were included. Wedge resections of the stomach and liver were not included to ensure a homogeneous cohort of patients who underwent major operations. Liver transplants were also not included. Patients with missing outcome measures, including LOS and discharge disposition, were excluded.

The primary dependent variable was OUD, which was identified by secondary ICD-9-CM diagnosis codes for opioid dependence (304.00–3, 304.70–3), opioid abuse (305.50–3), and opioid, heroin, or methadone overdose (965.00–2, 965.09, E850.0–1, E935.0–1). These diagnosis codes have been used in other similar studies, are included in the Healthcare Cost and Utilization Project statistical brief on hospitalizations for substance use disorders, and are consistent with the definition of OUD according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.[1,12,13,20] Although the codes do not distinguish OUD in treatment from active dependence/abuse, OUD can be considered a chronic relapsing condition, and a distinction was not made in this study.[21] Comparisons were made between patients with and without a documented history of OUD.

Variable Definitions

The outcomes measured were in-hospital complications, in-hospital mortality, LOS, and discharge disposition. Because patients are not identifiable or linked across multiple admissions, only inpatient complications and mortality could be captured and hospital readmissions could not be determined. In-hospital perioperative complications were defined using secondary ICD-9-CM diagnosis and procedure codes included in the Agency for Healthcare Research and Quality Patient Safety Indicators or that explicitly identify postoperative outcomes (Supplemental Digital Content 1, http://links.lww.com/SLA/B824).[22,23] Additionally, postoperative pain, delirium and confusion, and ileus and gastrointestinal complications have been assessed in other studies of OUD and were included.[12,13] A major complication was defined as any complication other than postoperative pain. Discharge disposition was categorized into routine (home or court/law enforcement), nonroutine (home healthcare, short-term hospital, skilled nursing or other facility, against medical advice), and alive but unknown destination.

Demographic and hospital characteristics included for analyses were patient age, sex, race (white, black, other), primary payer, patient residence (large metropolitan, small metropolitan, micropolitan, rural), income quartile, region (Northeast, Midwest, South, West), hospital bed-size (large, medium, small), hospital urban/rural location, and hospital teaching status, all of which were defined by the NIS. Missing data for each variable were included as a separate category for analyses.

Patient comorbidities were defined using the Elixhauser comorbidity index for administrative data, identifying as comorbidities secondary ICD-9-CM diagnosis codes that did not relate directly to the diagnosis-related group assignment for each patient.[24] Additionally, alcohol (291.0–5, 291.81–2, 291.89, 291.9, 303.00–3, 303.90–3, 305.00–3, 357.5, 425.5, 535.30–1, 571.0–3, E860.0) and nonopioid drug dependence and abuse were considered.[12,20] Nonopioid drugs included cannabis (304.30–3, 305.20–3), hallucinogens (304.50–3, 305.30–3, 969.9, E854.1, E939.6), sedatives and anxiolytics (304.10–3, 305.40–3), cocaine (304.20–3, 305.60–3, 968.5, 938.5), amphetamines (304.40–3, 305.70–3), antidepressants (305.80–3), and other unspecified substances (304.60–3, 304.80–3, 304.90–3, 305.90–3).

Statistical Analysis

National estimates were determined using weights provided by the NIS. Ninety-five percent confidence intervals (CI) of these estimates are included in supplemental tables (Supplemental Digital Content 2, http://links.lww.com/SLA/B825 and 3, http://links.lww.com/SLA/B826). Demographic characteristics are presented as frequencies for categorical variables and means with standard deviations for continuous variables. Statistical analyses for categorical and continuous variables were performed using the design-based Wald test and 2-sample *t*-test, respectively. Annual percent change in the proportion of patients classified as having OUD over time was calculated using linear regression with a logarithmically transformed dependent variable and year as a continuous independent variable. To determine the association between OUD and perioperative outcomes, propensity score matching was performed in the unweighted study population using a 1:2 "greedy" matching algorithm with a caliper distance of 0.2 of the standard deviation of the logit of the propensity score and controls used only once. Matching was performed using year of surgery, procedure type (esophagectomy, gastrectomy, hepatectomy, pancreatectomy), extent of resection (total or partial gastrectomy; Whipple procedure, total pancreatectomy, or other partial pancreatectomy), demographic variables, hospital characteristics, the presence of alcohol and non-opioid drug use disorders, and the number of nondrug-related Elixhauser comorbidities. The weighted matched cohorts were then compared using logistic regression for categorical outcomes (complications, mortality, discharge disposition) and 2-sample *t*-test for LOS. The Bonferroni method was used to adjust for multiple testing for subgroup analyses of specific perioperative complications. All tests were 2-sided. *P*-values <0.05 were considered statistically significant. Statistical analyses were performed using R version 3.5.3.[25]

RESULTS

Patient Characteristics

An estimated 376,467 patients underwent elective major upper abdominal surgery between 2003 and 2015, of which 1096 (0.3%) were documented as having OUD. Approximately 226,597 (95% CI 225,445–227,749; 60.2%) resections were performed for cancer. Patients with and without OUD differed significantly in multiple baseline characteristics (Table 1, Supplemental Digital Content 2, http://links.lww.com/SLA/B825). Compared to those without OUD, patients with OUD more frequently underwent pancreatectomy (47.6% vs 36.4%, $P < 0.001$), especially total pancreatectomy (20.4% vs 4.6%, $P < 0.001$). Additionally, patients with OUD were younger (mean 53 vs 61 years, $P < 0.001$) and more often male (55.1% vs 53.2%, $P < 0.001$), black (15.0% vs 7.6%, $P < 0.001$), Medicaid beneficiaries (22.0% vs 6.4%, $P < 0.001$), and in the lowest income quartile (32.6% vs 21.3%, $P < 0.001$). Alcohol (17.2% vs 2.8%, $P < 0.001$) and nonopioid drug (2.2% vs 0.2%, $P = 0.023$) dependence/abuse were also more prevalent among patients with OUD.

The proportion of patients documented as having OUD increased significantly over time with an annual percent change

TABLE 1. Characteristics of Patients Undergoing Major Upper Abdominal Surgery by Status of Opioid Use Disorder (OUD)

Characteristic	OUD N = 1096 (0.3%) N (%)	No OUD N = 375,371 (99.7%) N (%)	*P* value
Year of surgery, median (IQR)	2011 (2008–2014)	2009 (2006–2012)	<0.001
Procedure type			
Esophagectomy	77 (7.0)	39,042 (10.4)	<0.001
Gastrectomy	285 (26.0)	104,444 (27.8)	
Total	*68 (23.7[*])*	*36,724 (35.2[*])*	*0.025*
Partial	*217 (76.3[*])*	*67,720 (64.8[*])*	
Hepatectomy	212 (19.4)	95,403 (25.4)	
Pancreatectomy	522 (47.6)	136,483 (36.4)	
Whipple	*299 (57.4[†])*	*84,560 (62.0[†])*	*<0.001*
Total	*106 (20.4[†])*	*6317 (4.6[†])*	
Other partial	*116 (22.2[†])*	*45,605 (33.4[†])*	
Age			
<50 yr	353 (32.2)	69,903 (18.6)	<0.001
50–70 yr	662 (60.4)	192,539 (51.3)	
≥70 yr	82 (7.5)	112,929 (30.1)	
Sex			
Female	493 (44.9)	175,346 (46.7)	<0.001
Male	604 (55.1)	199,658 (53.2)	
Not reported	0 (0)	367 (0.1)	
Race/ethnicity			
White	686 (62.6)	242,515 (64.6)	<0.001
Black	164 (15.0)	28,485 (7.6)	
Other	87 (7.9)	46,987 (12.5)	
Not reported	159 (14.5)	57,385 (15.3)	
Primary payer			
Private	464 (42.3)	167,875 (44.7)	<0.001
Medicare	343 (31.3)	163,726 (43.6)	
Medicaid	241 (22.0)	23,959 (6.4)	
Other	48 (4.4)	19,202 (5.1)	
Not reported	0 (0)	609 (0.2)	
Patient residence			
Large metropolitan	637 (58.1)	196,292 (52.3)	0.086
Small metropolitan	270 (24.7)	108,399 (28.9)	
Micropolitan	106 (9.7)	39,211 (10.4)	
Rural	48 (4.4)	24,645 (6.6)	
Not reported	34 (3.1)	6824 (1.8)	
Income percentile			
0–25th	357 (32.6)	80,059 (21.3)	<0.001
26–50th	237 (21.6)	91,143 (24.3)	
51–75th	266 (24.2)	95,924 (25.6)	
76–100th	208 (18.9)	99,991 (26.6)	
Not reported	29 (2.6)	8254 (2.2)	
Region			
Northeast	232 (21.1)	85,164 (22.7)	0.083
Midwest	246 (22.5)	88,183 (23.5)	
South	348 (31.7)	133,962 (35.7)	
West	270 (24.7)	68,063 (18.1)	
Hospital bed-size			
Large	893 (81.5)	285,957 (76.2)	<0.001
Small or medium	203 (18.5)	88,115 (23.5)	
Not reported	0 (0)	1299 (0.3)	
Hospital location			
Urban	1058 (96.5)	363,234 (96.8)	<0.001
Rural	39 (3.5)	10,837 (2.9)	
Not reported	0 (0)	1299 (0.3)	
Hospital teaching status			
Teaching	884 (80.6)	301,638 (80.4)	<0.001
Nonteaching	212 (19.4)	72,433 (19.3)	
Not reported	0 (0)	1299 (0.3)	
Alcohol dependence/abuse	188 (17.2)	10,659 (2.8)	<0.001
Nonopioid drug dependence/abuse	24 (2.2)	778 (0.2)	0.023
Number of nondrug-related Elixhauser comorbidities, mean (SD)	2.7 (1.7)	2.2 (1.6)	<0.001

*Percent of patients undergoing gastrectomy.
†Percent of patients undergoing pancreatectomy.
CI indicates confidence interval; IQR, interquartile range; SD, standard deviation.

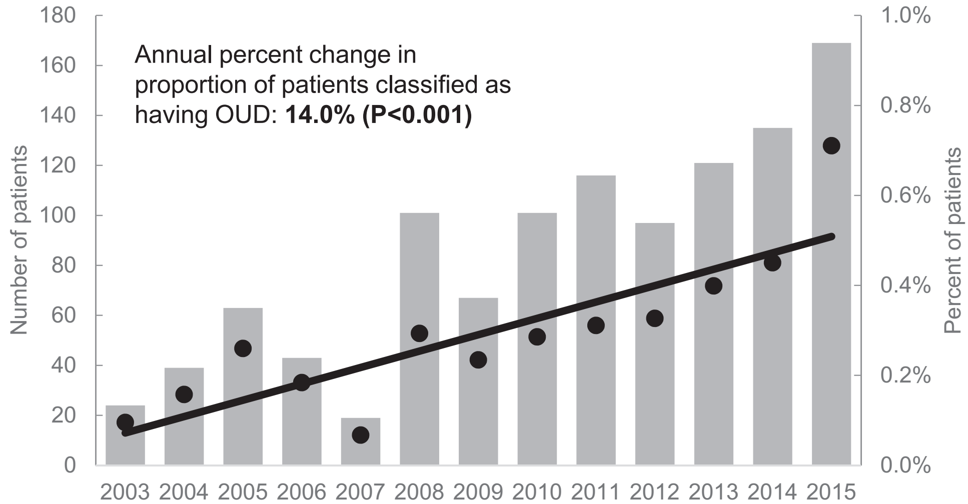


FIGURE 1. National estimates of the proportion of major upper abdominal surgery patients documented as having opioid use disorder (OUD).

of 14.0% ($P < 0.001$) (Fig. 1). In 2003, only 0.10% (95% CI 0.02%–0.17%) of patients undergoing major upper abdominal surgery were classified as having OUD. By 2015, the proportion had increased to 0.71% (95% CI 0.50%–0.92%).

Unadjusted Outcomes

The unadjusted perioperative outcomes are shown in Figure 2. Patients with OUD more frequently experienced in-hospital complications [52.9% vs 37.8%, odds ratio (OR) 1.8, 95% CI 1.5–2.3, $P < 0.001$], including postoperative pain (14.1% vs 4.0%, OR 3.9, 95% CI 2.8–5.5, Bonferroni-corrected $P < 0.001$), delirium and confusion (9.7% vs 2.2%, OR 4.7, 95% CI 3.1–6.9, Bonferroni-corrected $P < 0.001$), and pulmonary complications (19.4% vs 12.6, OR 1.7, 95% CI 1.2–2.2, Bonferroni-corrected $P = 0.008$). Furthermore, those with OUD more often required nonroutine disposition, including home healthcare or discharge to a nursing facility (48.9% vs 37.3%, OR 1.6, 95% CI 1.3–2.0, $P < 0.001$), and a longer LOS (mean 12.3 vs 10.7 days, $P = 0.010$). There was no significant difference in in-hospital mortality (2.6% vs 2.7%, OR 1.0, 95% CI 0.5–2.0, $P = 0.94$).

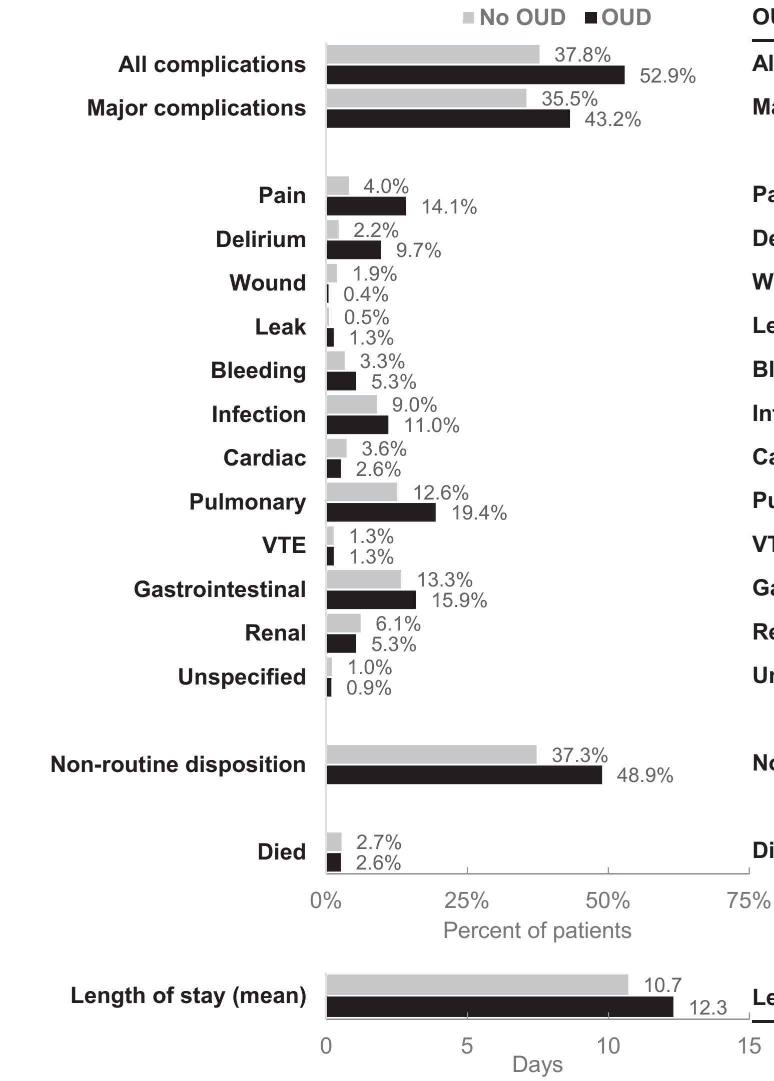
Propensity Score-matched Patients and Adjusted Outcomes

Propensity score matching resulted in an estimated 1077 (95% CI 951–1203) patients with OUD and 2164 (95% CI 1986–2342) patients without OUD. The measured baseline variables were better balanced and no longer differed significantly between groups (Table 2, Supplemental Digital Content 3, http://links.lww.com/SLA/B826, Supplemental Digital Content 4, http://links.lww.com/SLA/B827). Nevertheless, differences in perioperative outcomes persisted (Fig. 3). Patients with OUD were more likely to experience in-hospital complications (52.9% vs 37.3%, OR 1.9, 95% CI 1.4–2.5, $P < 0.001$), and major complications (43.5% vs 33.7%, OR 1.5, 95% CI 1.1–2.0, $P = 0.006$). Increased postoperative pain (13.9% vs 4.5%, OR 3.5, 95% CI 2.0–5.8, Bonferroni-corrected $P < 0.001$), delirium and confusion (9.9% vs 3.6%, OR 3.0, 95% CI 1.6–5.3, Bonferroni-corrected $P = 0.004$), and pulmonary complications (19.3% vs 10.5%, OR 2.0, 95% CI 1.4–3.0, Bonferroni-corrected $P = 0.006$) remained significantly associated with OUD. Additionally, patients with OUD more frequently experienced non-routine disposition (49.3% vs 37.2%, OR 1.6, 95% CI 1.2–2.2, $P < 0.001$) and longer LOS (mean 12.4 vs 10.6 days, $P = 0.015$). In-hospital mortality was somewhat higher in the OUD group, but this was not statistically significant (2.7% vs 1.1%, OR 2.4, 95% CI 0.8–7.1, $P = 0.10$).

DISCUSSION

Despite a rising prevalence of OUD in the United States, little is known regarding the impact of this disorder on perioperative outcomes after elective major upper abdominal surgery. Using data from a nationally representative sample of patients who underwent esophagectomy, total or partial gastrectomy, major hepatectomy, and pancreatectomy, we found that OUD was significantly associated with certain in-hospital complications. Additionally, patients with OUD experienced longer LOS and decreased rate of discharge to home after surgery.

The proportion of patients categorized as having OUD in the present study was 0.3%, comparable to the rates identified among orthopedic (0.2%) and cardiovascular (0.2%) surgery patients during a similar time period.[12,13] To our best knowledge, estimates of OUD prevalence in other general surgery populations have been limited. In a study by Ramchand et al published in 2009, the rate of illicit opioid use was found to be about 2% among patients treated at 4 trauma centers in Los Angeles County, but the study did not specifically evaluate OUD and relied on patient self-reporting.[26] The estimated proportion of patients documented as having OUD in the present study was somewhat lower than the prevalence of nonmedical prescription OUD (0.9%) and heroin use disorder (0.69%) among adults in the United States in recent epidemiologic studies.[16,17] The lower rates may be attributed in part to an older age distribution among these surgical patients, whereas OUD is typically more prevalent among younger adults.[3,16,17] The mean age was 61 years in the entire study population, and only 53 years among those with OUD. The proportion classified as having OUD in the present study also increased significantly from only 0.10% of study patients in 2003 to 0.71% in 2015. Although this trend may in part reflect increased prevalence of OUD in the general population over time,[16,17] there has also likely been improved awareness and documentation of the disorder among clinicians in more recent years.[2,7] The identification of comorbid conditions and complications in an administrative database is dependent upon accurate coding, and whereas coded comorbidities and complications in administrative



OUD vs. No OUD, OR (95% CI)		P value	P value*
All	1.8 (1.5-2.3)	<0.001	
Major	1.4 (1.1-1.7)	0.007	
Pain	3.9 (2.8-5.5)	<0.001	<0.001
Delirium	4.7 (3.1-6.9)	<0.001	<0.001
Wound	0.2 (0.04-1.3)	0.10	>0.99
Leak	2.6 (0.9-7.1)	0.071	0.85
Bleeding	1.7 (1.0-2.8)	0.056	0.67
Infection	1.3 (0.9-1.8)	0.23	>0.99
Cardiac	0.7 (0.3-1.5)	0.37	>0.99
Pulmonary	1.7 (1.2-2.2)	<0.001	0.008
VTE	1.0 (0.4-2.9)	0.94	>0.99
Gastrointestinal	1.2 (0.9-1.7)	0.21	>0.99
Renal	0.9 (0.5-1.4)	0.56	>0.99
Unspecified	0.8 (0.2-2.9)	0.79	>0.99
Non-routine	1.6 (1.3-2.0)	<0.001	
Died	1.0 (0.5-2.0)	0.94	
Length of stay		0.010	

FIGURE 2. Perioperative outcomes in all study patients with and without opioid use disorder (OUD). *Bonferroni-corrected *P* values. CI indicates confidence interval; OR odds ratio; VTE, venous thromboembolism.

data have been found to be fairly specific, they may be less sensitive compared to clinical records.[24,27,28] That is, whereas accurate, the true prevalence of underlying conditions such as OUD may be underestimated. On the other hand, it is unlikely that patients with low-level opioid use without dependence or abuse are included in the OUD group in this study, as the rate of preoperative opioid exposure among abdominopelvic surgery patients has been reported in the much higher range of 10%–20%.[14,15] Despite these limitations, administrative data provide valuable information on thousands of patients and relatively uncommon conditions, data that would otherwise be too costly or time-consuming to obtain.

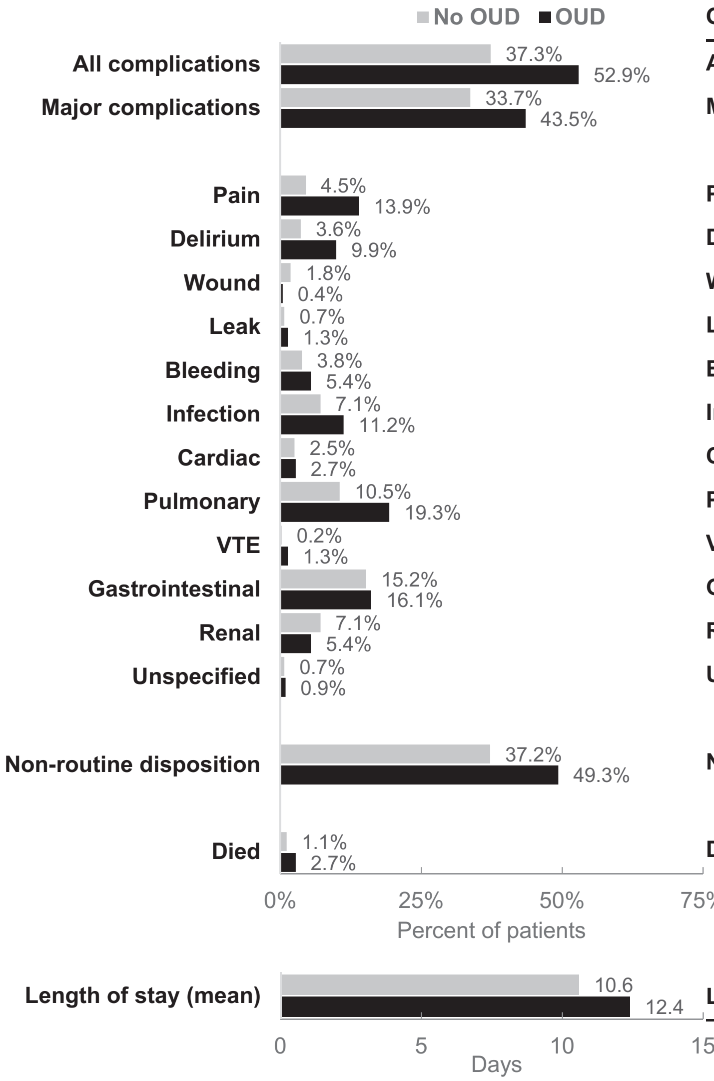
Patients with OUD represent a higher risk and more vulnerable population, including a high proportion of non-white racial groups, those in the lowest income quartile, and Medicaid beneficiaries.[16,17] The impact of race, socioeconomic status, and insurance coverage on healthcare access, treatment decisions, and postoperative outcomes have been well described across multiple clinical settings,[29–33] and could contribute to disparities in the perioperative care of patients with OUD. Additionally, clinicians should be aware that the co-occurrence of OUD with alcohol and non-opioid substance use disorders is common,[16,34] which could further complicate perioperative care.

Despite adjusting for differences in baseline characteristics between the OUD and non-OUD groups through propensity score matching, OUD remained significantly associated with increased postoperative pain, delirium and confusion, and pulmonary complications in the current study. Difficult pain control and higher perioperative narcotic requirements have previously been reported in patients with chronic opioid use or disorder.[8–11,13] These patients face several challenges that increase susceptibility to perioperative pain, including opioid-induced hyperalgesia, opioid tolerance and reduced efficacy, and opioid withdrawal and heightened stress response if substitution therapies (methadone, buprenorphine) are withheld.[35,36] Multimodal analgesia, including acetaminophen and nonsteroidal anti-inflammatory drugs, should be utilized to minimize narcotic requirements,[37,38] and epidural and other regional analgesia

TABLE 2. Characteristics of Propensity Score-matched Patients by Status of Opioid Use Disorder (OUD)

Characteristic	OUD N = 1077 N (%)	No OUD N = 2164 N (%)	*P* value
Year of surgery, median (IQR)	2011 (2008–2014)	2011 (2008–2013)	0.65
Procedure type			
Esophagectomy	77 (7.2)	121 (5.6)	0.85
Gastrectomy	285 (26.5)	575 (26.6)	
Total	*68 (23.7[*])*	*126 (21.8[*])*	*0.75*
Partial	*217 (76.3[*])*	*449 (78.2[*])*	
Hepatectomy	208 (19.3)	420 (19.4)	
Pancreatectomy	507 (47.1)	1048 (48.4)	
Whipple	*290 (57.1[†])*	*637 (60.8[†])*	*0.74*
Total	*101 (20.0[†])*	*203 (19.4[†])*	
Other partial	*116 (22.9[†])*	*208 (19.8[†])*	
Age			
<50 yr	338 (31.4)	599 (27.7)	0.17
50–70 yr	657 (61.0)	1323 (61.2)	
≥70 yr	82 (7.6)	241 (11.2)	
Sex			
Female	478 (44.4)	990 (45.8)	0.71
Male	599 (55.6)	1174 (54.2)	
Race/ethnicity			
White	676 (62.8)	1420 (65.6)	0.83
Black	159 (14.8)	304 (14.1)	
Other	87 (8.1)	174 (8.0)	
Not reported	155 (14.3)	266 (12.3)	
Primary payer			
Private	459 (42.6)	898 (41.5)	0.57
Medicare	343 (31.8)	778 (35.9)	
Medicaid	227 (21.1)	386 (17.9)	
Other	48 (4.5)	101 (4.7)	
Patient residence			
Large metropolitan	628 (58.3)	1198 (55.4)	0.60
Small metropolitan	266 (24.7)	536 (24.8)	
Micropolitan	106 (9.9)	227 (10.5)	
Rural	43 (4.0)	87 (4.0)	
Not reported	34 (3.1)	116 (5.4)	
Income percentile			
0–25th	338 (31.4)	589 (27.2)	0.45
26–50th	237 (22.0)	575 (26.6)	
51–75th	266 (24.7)	560 (25.9)	
76–100th	208 (19.3)	367 (17.0)	
Not reported	29 (2.7)	72 (3.3)	
Region			
Northeast	232 (21.5)	512 (23.8)	0.74
Midwest	237 (22.0)	502 (23.2)	
South	343 (31.8)	613 (28.3)	
West	266 (24.7)	536 (24.8)	
Hospital bed-size			
Large	879 (81.6)	1821 (84.2)	0.36
Small or medium	198 (18.4)	343 (15.8)	
Hospital location			
Urban	1038 (96.4)	2091 (96.7)	0.86
Rural	39 (3.6)	72 (3.3)	
Hospital teaching status			
Teaching	864 (80.3)	1729 (79.9)	0.90
Nonteaching	212 (19.7)	435 (20.1)	
Alcohol dependence/abuse	169 (15.7)	353 (16.3)	0.82
Nonopioid drug dependence/abuse	24 (2.2)	29 (1.3)	0.37
Number of nondrug-related Elixhauser comorbidities, mean (SD)	2.6 (1.6)	2.5 (1.7)	0.47

[*]Percent of patients undergoing gastrectomy.
†Percent of patients undergoing pancreatectomy.
IQR indicates interquartile range; SD, standard deviation.



OUD vs. No OUD, OR (95% CI)		P value	P value*
All	1.9 (1.4-2.5)	<0.001	
Major	1.5 (1.1-2.0)	0.006	
Pain	3.5 (2.0-5.8)	<0.001	<0.001
Delirium	3.0 (1.6-5.3)	<0.001	0.004
Wound	0.2 (0.04-1.6)	0.14	>0.99
Leak	2.0 (0.5-8.5)	0.34	>0.99
Bleeding	1.4 (0.7-2.8)	0.29	>0.99
Infection	1.6 (1.0-2.7)	0.048	0.58
Cardiac	1.1 (0.4-2.7)	0.84	>0.99
Pulmonary	2.0 (1.4-3.0)	<0.001	0.006
VTE	6.1 (0.8-46)	0.080	0.96
Gastrointestinal	1.1 (0.7-1.6)	0.72	>0.99
Renal	0.7 (0.4-1.4)	0.33	>0.99
Unspecified	1.3 (0.3-6.6)	0.72	>0.99
Non-routine	1.6 (1.2-2.2)	<0.001	
Died	2.4 (0.8-7.1)	0.10	
Length of stay		0.015	

FIGURE 3. Perioperative outcomes in propensity score-matched patients with and without opioid use disorder (OUD). *Bonferroni-corrected *P* values. CI indicates confidence interval; OR odds ratio; VTE, venous thromboembolism.

techniques may be explored.[35] Comprehensive care of this challenging population should include perioperative care coordination with anesthesia pain specialists.[39]

Associations between opioid use and postoperative delirium,[12] pneumonia,[12,14] respiratory failure or mechanical ventilation,[12–14] and increased LOS[9,12,13,15] have also previously been described. These complications may be related. Poor analgesia has been associated with cardiopulmonary complications.[39,40] Patients with uncontrolled pain may have poor pulmonary hygiene and thus susceptible to subsequent respiratory failure. Opioid exposure has also been associated with immunosuppression and increased risk of pneumonia and other infections in animal and clinical studies.[41,42] Understanding the relationship between opioid use and perioperative complications, whether related to pain or other systemic changes from chronic opioid exposure, require additional data.

Given the significant morbidities associated with major abdominal operations, surgeons and other providers should be educated on preoperative OUD screening. The rapid opioid dependence screen, an 8-item measure that can be quickly administered, has shown good positive and negative predictive values of 0.69 and 0.98, respectively.[43] OUD is also a modifiable risk factor, and initiation of OUD treatment could be considered before proceeding with surgery.[21] However, many patients undergo major abdominal resections for cancer, and significant delays that could lead to disease progression may not be favored. Additionally, for some patients, such as those with chronic pancreatitis, timely surgery could be important in pain management and long-term opioid reduction.[44,45] Even when OUD treatment is initiated, adherence may be imperfect, and OUD should thus be considered a chronic condition.[21] Regardless of whether OUD is treated preoperatively, patients should be closely monitored in the perioperative setting to mitigate potential adverse events.

Patients with OUD also had a high rate of non-routine discharge, requiring either home healthcare or discharge to a nursing facility. However, the specific reasons for a nonroutine discharge and the services these patients required post-discharge are not outlined in the NIS. Further studies are needed to better inform hospital administration and clinical decision-making. To develop an individualized plan for safe discharge and to prevent unplanned readmissions, social workers and discharge planners should be engaged early during the hospitalization.[46]

Several study limitations should be acknowledged. As with any retrospective study, causal relationships cannot be inferred. Although propensity score matching adjusted for differences in available baseline variables between the OUD and non-OUD groups, unobserved confounders likely persisted. For example, a strong volume-outcome relationship has been described for upper gastrointestinal and hepatopancreatobiliary operations.[22,47] After NIS redesign in 2012, empiric derivation of hospital volume is no longer possible.[48] However, propensity score matching adjusted for other hospital characteristics, such as bed-size and teaching status, that may be associated with surgical volume.[49] For the subset of study patients who underwent resections for malignancy, information on cancer stage and neoadjuvant therapies, which could impact perioperative outcomes, are not available in the NIS. Interaction between these factors and OUD in the setting of major abdominal surgery requires further investigation. The Elixhauser comorbidity index was used to define comorbid conditions. As with the concern that the true prevalence of OUD was under-represented in an administrative database, comorbidities may also not be fully captured.[24,27,28] Additionally, perioperative nutritional status, an important consideration in surgical outcomes, is not included in the Elixhauser index, although it does include recent weight loss.[24] Although there are limitations with using the Elixhauser index, in certain settings, it has been found to be superior to other comorbidity scores in its discriminative ability for postoperative outcomes.[50] Similarly, complications, although specific when included, may be under-reported, especially more subjective outcomes, such as poor pain control and delirium.[27,28] Moreover, because of the nature of the NIS database, post-discharge events, such as 30-day complication and readmission rates, could not be evaluated. Postoperative complications may be more reliably captured in clinical registries, such as the American College of Surgeons National Surgical Quality Improvement Program (NSQIP). Comparing the results from the current study to findings from NSQIP would be interesting, but OUD is currently not identified as a comorbidity in the NSQIP. Despite these limitations, the NIS provides valuable, clinically relevant information on the impact of OUD on perioperative outcomes after major upper abdominal surgery at a national population level.

In the context of the current opioid epidemic, healthcare providers should be aware of the specific needs and perioperative risks in patients with OUD. OUD, and the co-occurrence of other substance use disorders, should be assessed preoperatively. A multidisciplinary approach, with engagement of anesthesia pain specialists, and multimodal analgesia techniques should be utilized for better perioperative pain control in this population. Furthermore, patients with OUD should be closely monitored to mitigate potential adverse events, and patients' individualized discharge needs should be evaluated to ensure safe and timely discharge.

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