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Sohrab Arora
Henry Ford Health, sarora3@hfhs.org

Chandler Bronkema
Henry Ford Health, cbronke1@hfhs.org

Sami E. Majdalani
Henry Ford Health, smajdal1@hfhs.org

Nicholas Corsi
Henry Ford Health, ncorsi1@hfhs.org

Ivan Rakic
Henry Ford Health, irakic1@hfhs.org

See next page for additional authors

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Authors
Sohrab Arora, Chandler Bronkema, Sami E. Majdalani, Nicholas Corsi, Ivan Rakic, Austin J. Piontkowski, Akshay Sood, Matthew Davis, Daniele Modonutti, Giacomo Novara, Craig G. Rogers, and Firas Abdollah

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ORIGINAL ARTICLE

Impact of preexisting opioid dependence on morbidity, length of stay, and inpatient cost of urological oncological surgery

Sohrab Arora[1,2] · Chandler Bronkema[1] · Sami E. Majdalany[1] · Nicholas Corsi[1,3] · Ivan Rakic[1,3] · Austin Piontkowski[1,3] · Akshay Sood[1,4] · Matthew J. Davis[1] · Daniele Modonutti[1,5] · Giacomo Novara[5] · Craig G. Rogers[2] · Firas Abdollah[1,2,3]

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Abstract

Objectives To determine the incidence of preexisting opioid dependence in patients undergoing elective urological oncological surgery. In addition, to quantify the impact of preexisting opioid dependence on outcomes and cost of common urologic oncological procedures at a national level in the USA.

Methods We used the National Inpatient Sample (NIS) to study 1,609,948 admissions for elective partial/radical nephrectomy, radical prostatectomy, and cystectomy procedures. Trends of preexisting opioid dependence were studied over 2003–2014. We use multivariable-adjusted analysis to compare opioid-dependent patients to those without opioid dependence (reference group) in terms of outcomes, namely major complications, length of stay (LOS), and total cost.

Results The incidence of opioid dependence steadily increased from 0.6 per 1000 patients in 2003 to 2 per 1000 in 2014. Opioid-dependent patients had a significantly higher rate of major complications (18 vs 10%; $p < 0.001$) and longer LOS (4 days (IQR 2–7) vs 2 days (IQR 1–4); $p < 0.001$), when compared to the non-opioid-dependent counterparts. Opioid dependence also increased the overall cost by 48% (adjusted median cost $18,290 [IQR 12,549–27,715] vs. $12,383 [IQR 9225–17,494] in non-opioid-dependent, $p < 0.001$). Multivariable analysis confirmed the independent association of preexisting opioid dependence with major complications, length of stay in 4th quartile, and total cost in 4th quartile.

Conclusions The incidence of preexisting opioid dependence before elective urological oncology is increasing and is associated with adverse outcomes after surgery. There is a need to further understand the challenges associated with opioid dependence before surgery and identify and optimize these patients to improve outcomes.

Keywords National inpatient sample · Urologic neoplasms · Cost · Opioid dependence · Surgery

Introduction

Over the last few decades, opioid use has reached an epidemic status in the USA. In 2015, the Centers for Disease Control attributed a total healthcare expenditure of $501 billion to this problem [1]. It has been described as a "crisis" in the media and a "public health emergency" by the White House [2]. As a backwash of this crisis, we see many patients already using prescription opioids at the time of surgical evaluation for urological disorders.

While recent literature has focused on postoperative opioid use, there are limited data on the outcomes of patients who are already opioid-dependent and need elective urological surgery. This is a potentially high-risk surgical population who might need tailored perioperative care. Opioid use has well-known effects on pain control [3], respiratory function, and gastrointestinal function4, in

✉ Firas Abdollah
fabdoll1@hfhs.org

1 Vattikuti Center for Outcomes Research, Analytics and Evaluation, Henry Ford Hospital, Detroit, MI, USA

2 Vattikuti Urology Institute, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI 48202-2689, USA

3 Wayne State University School of Medicine, Detroit, MI, USA

4 Department of Urology, University of Texas MD Anderson Cancer Center, Houston, TX, USA

5 Department of Oncological and Surgical Sciences, Urology Clinic, University of Padova, Padua, Italy

addition to complex underlying emotional and psychological issues [5].

In surgical patients, preexisting opioid use has been associated with increased length of stay, healthcare costs, and morbidity after abdominal [6], cardiac [7], and orthopedic [8–10] surgeries. Interestingly, this is a potentially modifiable factor to consider during optimization, especially for major oncological procedures. Most notably, Nguyen et al. showed improved pain and functional outcomes even after a 50% reduction in preoperative opioid burden [11]. As such, this is a potentially high-yield target for surgical optimization. Defining risk and economic impact in patients with preexisting opioid dependence is also critical in the context of value-based reimbursement models for access to opioid use disorder treatment [12].

In this study, we sought to ascertain the incidence of preexisting opioid dependence in patients undergoing elective urological oncological surgery. We also aimed to quantify the impact of preexisting opioid dependence on outcomes and cost of common urologic oncological procedures at a national level in the USA.

Methods

Data source

The United States (US) Healthcare Cost and Utilization Project (HCUP) National Inpatient Sample (NIS) is the largest publicly available, all-payer, inpatient care database in the country. This database constitutes a 20% stratified sample of hospital discharges from all US community hospitals [13]. Stratified sampling allows for generation of national estimates from these data using HCUP-provided survey weights [14].

Study population

We focused on 1,609,948 (per NIS survey weights [14]) admissions for elective partial nephrectomy, radical nephrectomy, radical prostatectomy, and cystectomy procedures for non-metastatic disease in adult patients (age > 18) within the NIS between 2003 and 2014. This study period was chosen as the database switched to ICD-10 codes from 2015 onward. For each record, preexisting opioid abuse/dependence was identified using International Classification of Diseases, Ninth Revision (ICD-9) codes 304.00, 304.01. 304.02, 304.03, 304.70, 304.73, 305.50–53, per HCUP statistical brief #177. [15]

Covariates

For each record, patient characteristics abstracted included age, gender, race (white, black, or other), Charlson comorbidity score (0–2, 3–5, and > 5) [16], smoker/non-smoker, diagnosis of acquired immunodeficiency syndrome, type of admission (elective/non-elective), primary payer (state/private/other), urban/semi-urban/rural location, zip code-based income quartiles, year of surgery, and hospital characteristics, namely teaching status, hospital location (rural or urban), and hospital region (Northeast, Midwest, South, or West).

Outcomes

The outcomes studied were:

1. Major inpatient complications, coded as having at least one complication and a length of stay greater than the 75th percentile for the specific procedure; methodology previously described [17–19]. The complications were coded using ICD-9 diagnosis and procedure codes [17, 19].
2. Length of stay (LOS) in days
3. Total inpatient cost: This was calculated using HCUP cost-to-charge files. The cost was adjusted to 2014 US Dollars using HCUP consumer price index [20].

"High LOS" and "high total cost" were then categorized as the upper quartile of LOS and total inpatient cost, respectively, and coded separately for each procedure and year. Of note, any complication was also reported for descriptive purposes only.

Statistical methodology

First, trends in preoperative opioid dependence were studied using HCUP-provided trend weights and design-corrected weighted least-squares linear regression. Second, complex survey procedures were used to compare patients with opioid dependence to those without opioid dependence (reference group) in terms of the covariates mentioned above. Hospital counts and records were scaled using HCUP-provided survey weights to make inferences at the national level. Third, the two populations were compared in terms of any complications, major complications, LOS, and total inpatient cost. Finally, multivariable logistic regression—using generalized estimating equation framework to account for sample weights—tested the impact of opioid dependence on major complications, high LOS, and high total cost. This model was adjusted for year of surgery, specific procedure, and patient and hospital characteristics, namely age, race, sex, Charlson comorbidity score, location, hospital teaching status, hospital region, and median zip code income quartiles. A generalized estimating equation framework accounts for the nesting effect (as there could be clustering of outcomes for patients undergoing surgery at the same hospital). The analysis was performed using SAS software, version 9.4 (SAS Institute Inc., Cary, NC). All tests were performed 2-sided.

Results

A total of 1835 (0.1%) records included a diagnosis of opioid dependence. Incidence of opioid dependence steadily increased from 0.6 per 1000 patients in 2003 to 2 per 1000 patients in 2014 ($p<0.001$; Fig. 1). Opioid dependence was more common in younger patients (median age 53 [IQR 45–58] vs 61 [IQR 53–67] in reference group; $p<0.001$; Table 1). Although most of the patients were white in both groups, the opioid-dependent group had a higher proportion of black patients (15 vs 9% in the reference group; $p<0.001$). There was no significant difference in gender distribution (females 23 vs 22% in the reference group; $p=0.6$). Opioid-dependent patients were more likely to be on Medicare/Medicaid (56 vs 41% in the reference group; $p<0.001$). The proportion of opioid-dependent patients was higher in cystectomy (2.1/1000) and nephrectomy patients (1.8/1000) compared to prostatectomy (0.4/1000) group.

As shown in Table 2, opioid-dependent patients had a significantly higher rate of major in-hospital complications (18% vs 10% in reference; $p<0.001$), any complications (26 vs 20%; $p<0.001$), blood transfusion (18 vs 11%; $p<0.001$), hemorrhage (6 vs 4%; $p=0.008$), and postoperative infection (2 vs 1%; $p=0.01$).

The LOS was significantly longer in opioid-dependent vs in reference group (4 days [IQR 2–7)] vs 2 days [IQR 1–4]; $p<0.001$). The adjusted median cost was $18,290 (IQR 12,549–27,715), which is 48% higher than $12,383 (IQR 9,225–17,494) in reference group ($p<0.001$). Opioid-dependent patients were more likely to be discharged to a facility (22% vs 12% in reference group, $p<0.001$).

On multivariable analysis, after taking into account the year of surgery, and the procedure, opioid dependence

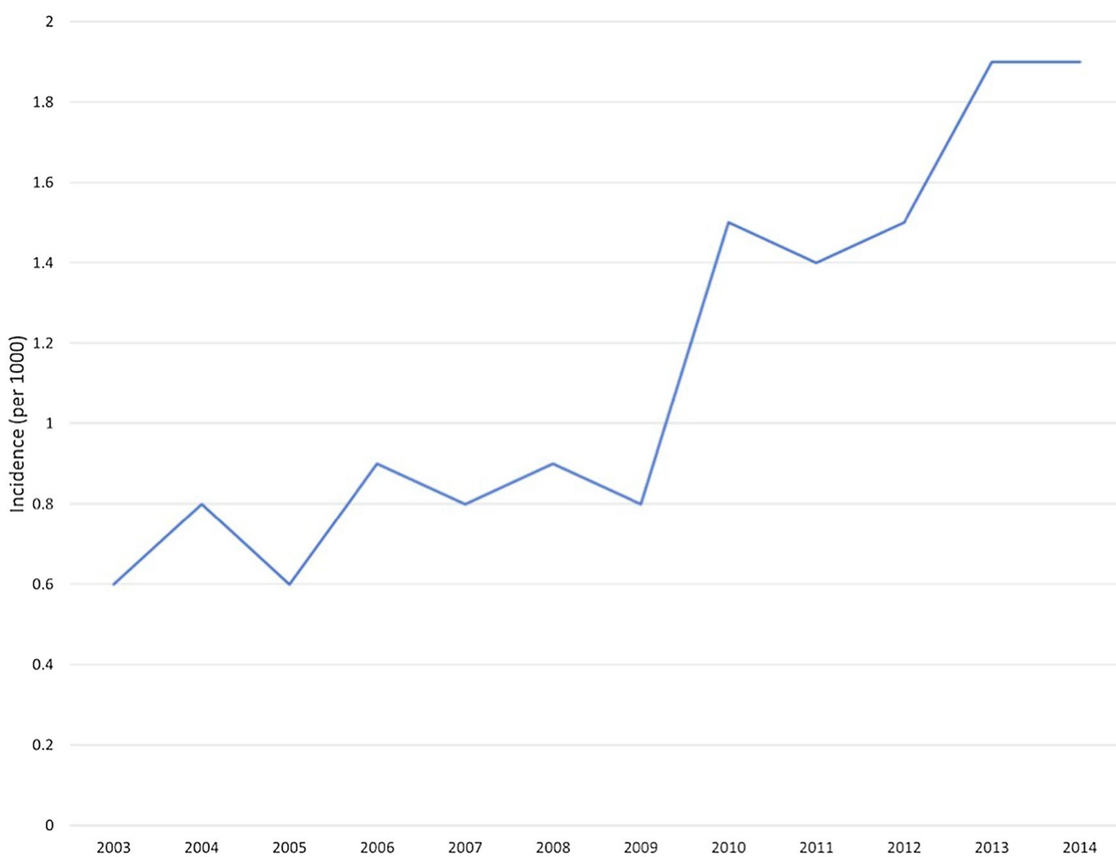

Fig. 1 Incidence of pre-existing opioid dependence in patients undergoing elective partial/radical nephrectomy, radical prostatectomy, and cystectomy procedures in the United States from 2003-2014. $P<0.001$, using design-corrected weighted least-squares linear regression

Table 1 Descriptive characteristics of 1,609,948 adult patients undergoing partial nephrectomy, radical nephrectomy, radical prostatectomy, and cystectomy procedures from 2003 through 2014 within the National Inpatient Sample, stratified by opioid dependence status

Variable	Entire cohort (*n* = 1,609,948)	Non-opioid-dependent patient (*n* = 1,608,113)	Opioid-dependent patients (*n* = 1,835)	*p*
Age, median (IQR), years	61 (53–67)	61 (53–67)	53 (45–58)	< 0.001
Female, *n* (%)	346,921 (21.7)	372,168 (21.7)	420 (22.9)	0.6
Race, *n* (%)				
White	1,015,959 (63.1)	1,014,924 (63.1)	1035 (56.4)	0.001
Black	148,458 (9.2)	148,189 (9.2)	270 (14.7)	
Other	445,531 (27.7)	445,000 (27.7)	530 (28.9)	
Charlson comorbidity score, *n* (%)				
0–2	1,186,380 (73.7)	1,185,122 (73.7)	1259 (68.6)	< 0.001
3–5	388,078 (24.1)	387,600 (24.1)	477 (26.0)	
≥ 6	35,490 (2.2)	35,391 (2.2)	99 (5.4)	
Smoker, *n* (%)	169,117 (10.5)	168,421 (10.5)	695 (37.9)	< 0.001
AIDS, *n* (%)	938 (0.06)	914 (0.06)	24 (1.3)	< 0.001
Elective admission, *n* (%)				
No	149,051 (9.3)	148,642 (9.3)	409 (22.3)	< 0.001
Yes	1,457,263 (90.7)	1,455,837 (90.7)	1426 (77.7)	
Primary payer, *n* (%)				
State (Medicare/Medicaid)	665,331 (41.0)	664,309 (41.4)	1022 (55.7)	< 0.001
Private	833,628 (52.0)	833,073 (52.0)	555 (30.3)	
Other	105,803 (6.6)	105,546 (6.6)	257 (14.0)	
Location, *n* (%) **				
Urban	556,161 (40.1)	555,304 (40.1)	856 (52.9)	< 0.001
Semi-urban	423,552 (30.6)	423,184 (30.6)	367 (22.7)	
Rural	406,103 (29.3)	405,707 (29.3)	396 (24.5)	
Median zip code income quartile, *n* (%)				
Quartile 1	332,310 (21.1)	331,723 (21.2)	587 (33.1)	< 0.001
Quartile 2	382,791 (24.3)	382,337 (24.3)	454 (25.6)	
Quartile 3	411,935 (26.2)	411,496 (26.2)	439 (24.8)	
Quartile 4	445,120 (28.3)	444,829 (28.3)	291 (16.4)	
Teaching hospital, *n* (%)	798,446 (65.1)	797,571 (65.1)	875 (75.4)	0.001
Hospital location, *n* (%)				
Rural	66,322 (5.4)	66,283 (5.4)	39 (3.3)	0.2
Urban	1,160,848 (94.6)	1,159,727 (94.6)	1121 (96.7)	
Hospital region, *n* (%)	283,356 (19.1)	282,954 (19.1)	402 (25.1)	< 0.001
Northeast Midwest	355,106 (23.9)	354,796 (23.9)	311 (19.4)	
South	536,374 (36.2)	536,002 (36.2)	371 (23.2)	
West	308,682 (20.8)	308,166 (20.8)	516 (32.2)	
Procedure, *n* (%)				
Radical/partial nephrectomy	719,040 (44.7)	717,766 (44.6)	1274 (69.4)	< 0.001
Radical prostatectomy	784,057 (48.7)	783,719 (48.7)	338 (18.4)	
Cystectomy	106,851 (6.6)	106,628 (6.6)	223 (12.2)	

IQR Interquartile range, *AIDS* acquired immunodeficiency syndrome

*Facility: Skilled Nursing Facility, Intermediate Care Facility, Another Type of Facility, Home Health Care

**Urban, defined as patient location in counties of metro areas of 41 million population; semi-urban, defined as patient location in counties of metro areas of populations of 50,000 to 999,999; and rural, defined as those living in micropolitan or smaller counties

was independently associated with major complications (odds ratio [OR] 1.52; 95% confidence intervals [CI] 1.05–2.19), length of stay > = 4th quartile (OR 2.22 [95% CI 1.68–2.94]), and total inpatient cost > = 4th quartile (OR 2.12 [95% CI 1.57- 2.84]) (see Supplementary Tables 1, 2, and 3).

Table 2 Patient outcomes, length of stay, and cost of 1,609,948 adult patients undergoing partial nephrectomy, radical nephrectomy, radical prostatectomy, and cystectomy procedures stratified by opioid dependence status

Variable	Entire cohort (n = 1,609,948)	Non-opioid-dependent patient (n = 1,608,113)	Opioid-dependent patients (n = 1835)	p
Major complication, n (%)	154,779 (9.6)	154,443 (9.6)	336 (18.3)	< 0.001
Any complication, n (%)	303,384 (18.8)	339,686 (20.1)	479 (26.0)	< 0.001
Blood transfusion, n (%)	168,916 (10.5)	168,584 (10.5)	332 (18.1)	< 0.001
Digestive, n (%)	70,719 (4.4)	70,634 (4.4)	85 (4.7)	0.8
Hemorrhage, n (%)	59,826 (3.7)	59,712 (3.7)	113 (6.2)	0.01
Respiratory, n (%)	24,123 (1.5)	24,077 (1.5)	46 (2.5)	0.1
Urinary, n (%)	17,912 (1.1)	17,897 (1.1)	15 (0.8)	0.6
Post-op infection, n (%)	11,953 (0.7)	11,919 (0.7)	34 (1.9)	0.01
Wound, n (%)	6347 (0.4)	6337 (0.4)	10 (0.6)	0.6
Vascular, n (%)	*	*	*	*
Cardiac, n (%)	*	*	*	*
Other, n (%)	*	*	*	*
Inpatient death, n (%)	*	*	*	*
Parenteral nutrition, n (%)	16,257 (1.2)	16,211 (1.0)	46 (2.5)	< 0.001
Length of stay, median (IQR), days	2 (1–4)	2 (1–4)	4 (2–7)	< 0.001
Adjusted cost, 2014 USD, median (IQR)	12,387 (9,227-17,506)	12,383 (9,225-17,494)	18,290 (12,549-27,715)	< 0.001
Disposition (not including death), n (%)	397,960 (86.8)	1,396,549 (86.8)	1411 (76.9)	
Routine	*	*	*	< 0.001
Short-term hospital	196,328 (12.2)	195,934 (12.2)	394 (21.5)	
Other facility*	12,178 (0.8)	12,153 (0.8)	24 (1.4)	
Other/unknown				

Discussion

In this comprehensive study using a national database, we found that the incidence of preexisting opioid dependence in patients having elective surgery for urologic oncological procedures is increasing in the USA; there was an almost 300% increase during our study period. The above trend is expected, but concerning, given the elevated risk for worse outcomes in these patients as found in our study. In 2014, the incidence of preexisting opioid dependence in our study was 0.2%. This is lower than that reported for orthopedic (spine) procedures at 0.9% [8] and lower extremity bypass procedures at 0.6% [21], but consistent with 0.4% reported for total hip and knee arthroplasty by Wilson et al. [8], and 0.5% reported for urological procedures by Doan et al. [22]. Of note, Doan et al. included all patients taking long-term opioids, not only those who were dependent on opioids. The lower number in our study may also be reflective of the older age of presentation of patients with urological cancers. Opioid dependence is more commonly seen in younger population, as we also noted in our study. While the above numbers are sobering, they may represent a tip of an iceberg as we included only opioid-dependent patients, and not all patients who were using opioids at the time of surgery, which may be as high as 21% [6].

We demonstrated an independent association between preexisting opioid dependence and major complications after adjusting for the type of procedure, year of surgery, and patient and hospital characteristics. Higher rate of infectious complications in our study (Table 2) can be explained by the known inhibitory effect of opioids on immune function [23]. Interestingly, opioid-dependent patients also had a higher risk of hemorrhage and blood transfusion. This association has not been described in the literature and warrants further evaluation. It is possible that opioid-dependent patients present at a more advanced disease stage, resulting in higher blood loss. Unfortunately, the NIS database does not include disease characteristics, and this remains a speculation.

Opioid dependence not only increased the morbidity, but was also independently associated with increased LOS and augmented the overall cost per admission by 48%. This can partly be explained by the higher major complication rate in opioid-dependent patients. However, there may be other factors driving LOS and costs. For example, opioid-tolerant patients may experience more pain postoperatively, especially in the first 24 to 48 hours [24]. Inadequate pain control can delay surgical milestones [25] like adequate ambulation, which can increase the risk of longer hospital stay. Additionally, ineffective coping mechanisms, psychosocial issues, and fear of mistreatment may contribute to delayed discharge in these patients, further contributing to increased inpatient costs. Detailed evaluation is needed to identify potential targets for surgical quality improvement in this regard.

The American Urological Association recommends carefully considering "altering the pain management in those already taking opioids regularly for chronic pain or addiction treatment" [26]. The association also encourages involving input from the patient's caregivers and pain and addiction specialists, in addition to relying on multimodal agents for pain control in these patients. It is important to note that optimization of these patients before surgery presents a low-hanging fruit for quality improvement, not unlike tobacco cessation and nutritional rehabilitation. Nguyen et al. showed that even a 50% reduction in preoperative opioid burden has been associated with improved clinical, pain, and functional outcomes after total joint arthroplasty [11]. Interestingly, in this study, the authors reported that opioid use was the second most preoperative variable of concern to surgeons in the context of optimization before elective surgery.

Despite robust statistical analysis, methodology consistent with the existing literature [7], and adequate sample size, the findings in our study should be interpreted within the limitations of the retrospective and observational study design, and limitations of administrative datasets. Post-discharge events are not captured within the NIS, which means that our study likely underestimated the complication rates. The costs outside of admission, including costs of rehabilitation, and other facilities, readmission, etc., are not represented in this study. There may be under coding of opioid dependence as the providers are often reluctant to assign such diagnoses to patients, which also highlights the fact that our numbers may be the tip of an iceberg. The NIS also does not include disease characteristics like tumor stage and histology. However, surgical procedural codes are likely accurate as they are claim-based. Despite the limitations, our study provides a first snapshot of this problem at a national level in uro-oncological patients and adds to the growing body of evidence on this subject.

Conclusions

In this study, we found that preexisting opioid dependence before elective partial/radical nephrectomy, radical prostatectomy, and cystectomy is becoming increasingly common. Preexisting opioid use is associated with higher major complication rate, increased length of stay, and 48% increase in in-hospital costs. This underlies the need to better understand the challenges associated with opioid dependence before surgery, identify, optimize, and appropriately counsel these patients to improve outcomes.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00345-023-04306-1.

Data availability The National Inpatient sample data is publically available. We are not able to share the data, as it can be shared with those working on the project, and have signed a data use agreement with HCUP.

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