Title
Implementing an opioid reduction protocol in renal transplant recipients

Permalink
https://escholarship.org/uc/item/3sx9b2zm

Journal
The American Journal of Surgery, 220(5)

ISSN
0002-9610

Authors

Schwab, Marisa E
Braun, Hillary J
Ascher, Nancy L
et al.

Publication Date
2020-11-01

DOI
10.1016/j.amjsurg.2020.06.055

Peer reviewed

Implementing an Opioid Reduction Protocol in Renal Transplant Recipients

Marisa E. Schwab, MD[1,*], **Hillary J. Braun, MD**[1,*], **Nancy L. Ascher, MD PhD**[1], **Ryutaro Hirose, MD**[1,§]

[1]Department of Surgery, Division of Transplantation, University of California San Francisco, CA, USA

Sentence summary

Opioid dependence after renal transplantation is associated with an increased risk of graft loss and death. We implemented a protocol in renal transplant recipients that eliminated routine opioid patient-controlled analgesia and included non-opioid adjuncts. This protocol increased the use of non-opioid adjuncts but did not significantly decrease the amount of opioids prescribed at discharge. Most patients were still prescribed opioids at discharge in excess of what they required immediately prior to discharge.

Keywords

Renal transplantation; Opioids; PCA

Introduction

Opioid consumption during a patient's hospitalization has been directly linked to future opioid dependence. In the surgical population, 6% of opioid-naïve patients develop new opioid dependence post-operatively.[1] It has also been shown that renal transplant recipients who fill opioid prescriptions for 90 days in the first year after transplant have an increased risk of death and graft loss.[2] In light of these findings, it is critically important to the transplant community to find ways to minimize opioid use in the post-transplant setting.

One opioid delivery system commonly used is the patient-controlled analgesia (PCA) pump. The PCA was developed in the 1960s based on the hypothesis that patients would experience less pain and anxiety if they had control over their pain medication.[3] Since their introduction, PCAs have become widely used in the post-operative setting across the United States. While PCA use has been associated with improved patient satisfaction, it also correlates with an increased opioid consumption during the hospitalization and an unchanged length of hospitalization in post-operative patients.[4] As the opioid crisis continues to demonstrate a devastating impact on addiction and overdoses throughout the

§**Corresponding Author**: Dr. Ryutaro Hirose, MD, Professor of Surgery, Division of Transplant, University of California, San Francisco, Box 0780, 505 Parnassus Avenue, M884, San Francisco, CA 94117, Phone: (415) 353-8615, Fax: (415) 353-8974, ryutaro.hirose@ucsf.edu.
*Co-first authors

United States, minimizing opioids in surgical patients is paramount.[1] We postulated that renal transplantation would mirror other surgical specialties where it has been demonstrated that common surgical procedures are associated with an increased risk of chronic opioid use following discharge.[5]

The purpose of this study was to examine the impact of PCA elimination and the introduction of non-opioid adjuncts on opioid requirements at discharge in renal transplant recipients, at a single high volume transplant center. The amount of opioids prescribed at discharge was evaluated using the classification system described by Hill et al. which characterizes the needs of post-operative patients based on the number of opioid pills received on the day prior to discharge; this has previously been shown to satisfy the outpatient pain needs of 85% of patients.[6]

Material and methods

Institutional Review Board approval was obtained from the University of California, San Francisco Committee on Human Research (IRB #19–29209).

A clinical pain protocol was developed which removed the automatic post-operative order for a PCA pump and prescribed an opioid-sparing, multimodal pain control regimen after renal transplantation. This included scheduled Tylenol, Lidocaine patches, and Gabapentin. The protocol detailed in a stepwise fashion which opioids should be prescribed post-operatively, allowing opioids for uncontrolled pain. If the patient's pain continued to be uncontrolled, a PCA pump could then be prescribed. This protocol was circulated to all providers and nurses in the transplant unit and education was provided to staff in the post-anesthesia care unit as necessary. The protocol was instituted for all adult recipients of a living or deceased donor renal transplant at our institution beginning in June 2019. After the protocol was initiated, a two-week adjustment period was allowed prior to data collection. A retrospective chart review was then performed for the three months prior to protocol initiation (March, April, May 2019) and the three months following protocol implementation (July, August, September 2019). Additionally, we performed a retrospective chart review of patients who received a renal transplant during a "long-term study period", defined as seven months after protocol initiation (February 2020), to assess whether providers continued to follow the protocol over time. Manual review was used to collect the following: patient demographics, history of pre-operative opioid use, operative details, duration and usage of PCA (if applicable), length of hospitalization, oral morphine equivalents (OMEs) on the day prior to discharge, and OMEs prescribed at discharge. OMEs were translated into number of pills, where 1 pill was defined as one Oxycodone 5mg tablet.

The number of opioid pills prescribed *on the day prior to discharge* were categorized according to the classification by Hill et al.: A) 0 pills, B) 1–3 pills, and C) 4 pills.[6] The recommendation for opioid prescription *at discharge* is as follows: 0 pills for group A, 15 pills for group B, and 30 pills for group C.[6]

Patients were excluded if they received an intra-abdominal transplant, simultaneous pancreas renal transplant, or had a pre-existing diagnosis of chronic pain. Patients with chronic

pain were defined as those who were prescribed opioids on a regular basis prior to transplantation. Statistical analysis was performed using R software (version 1.2.5019). Pre-protocol era and post-protocol era metrics were compared using Mann Whitney tests, Chi squared tests, and Pearson correlations where applicable, with statistical significance set at $p < 0.05$.

Results

One hundred sixty-nine patients received a living or deceased donor renal transplant during the study period. Eleven percent (n=19) had a history of chronic pain and were thus excluded from the analysis. One hundred and fifty patients were included, with 79 in the pre-protocol implementation era and 71 in the post-protocol implementation era.

Demographics

The median patient age was 54 (range 20–80 years old), and 48.7% were female, with no significant differences between the pre- and post- groups (Table 1). There was a significant difference in race/ethnicity between the pre-protocol and post-protocol eras; the majority of the pre-protocol era patients were Asian (30.4%, n=24) and the majority of the post-protocol era patients were White (28.2%, n=20) . Patients were transplanted by one of ten surgeons at our institution. The most common indications for renal transplant were diabetes (28.7%, n=43) and hypertension (18.7%, n=28).

Opioids during the hospitalization

There was no significant difference in the amount of opioids given intra-operatively between the pre-protocol era and post-protocol era patients. Pre-protocol patients received a median of 225 OMEs intra-operatively, versus post-protocol patients who received a median of 200 OMEs (p-value 0.07).

Prior to the implementation of the new pain protocol, 81% (n=64) of renal transplant recipients received a PCA pump. After the protocol was introduced, only 4.2% (n=3) of the "post-protocol era" patients were prescribed a PCA (p<0.001). During the pre-protocol era, patients received a median of 220 mcg of fentanyl from the PCA. During the post-protocol era, the 3 patients who required a PCA received a median of 150 mcg of fentanyl (p-value 0.6).

During the post-protocol era, gabapentin prescriptions increased from 6.3% to 69% (p<0.001), while topical lidocaine use increased from 5.1% to 66.2% (p<0.001), and acetaminophen increased from 73.4% to 93% (p-value 0.003, Figure 1).

During the "long-term study period", 19 patients underwent renal transplantation and none were prescribed a PCA.

Opioids at discharge

To assess the impact of PCA use on discharge medications, we compared patients who utilized PCA analgesia versus those who did not, regardless of pre or post-protocol era. The median amount of opioids received on the day prior to discharge was 7.5 OMEs in the PCA

group and 5 OMEs in the non-PCA group (p-value 0.11). The median amount of opioids prescribed upon discharge was 75 OMEs in the PCA group and 75 OMEs in the non-PCA group (p-value 0.06). The median length of hospitalization was similar in both groups: 4 days in the PCA group and 3 days in the non-PCA group (p-value 0.08).

Patients were further categorized into one of three groups based on the number of opioid pills received on the day prior to discharge, according to Hill et al's classification,[6] irrespective of whether they received a PCA (Figure 2). Group A received 0 pills on the day prior to discharge and made up 36.7% of the pre-protocol era patients and 42.3.% of the post-protocol era patients. Group B received 1–3 pills on the day prior to discharge and made up 41.8% of pre-protocol era patients and 42.3% of post-protocol era patients. Group C received 4 pills on the day prior to discharge and made up 16.5% of pre-protocol era patients and 14.1% of post-protocol era patients

The number of opioids prescribed at discharge was analyzed for each of the three groups (Figure 3), again irrespective of whether they had received a PCA. Group A should have been prescribed 0 pills at discharge, per Hill's classification[6]: 50% of pre-protocol era and 35.5% of post-protocol era patients were prescribed excessive opioids (more than 0) at discharge (Figure 3). Group B should have been prescribed 15 pills at discharge per the classification: 24.3% of pre-protocol era and 25.8% of post-protocol era patients were prescribed excessive opioids (more than 15) at discharge (Figure 4). And group C should have been prescribed 30 pills at discharge per the classification: only one patient in the pre-protocol era was prescribed excessive opioids (more than 30) at discharge (Figure 5).

Discussion

Post-operative opioid use is a significant problem in the United States, however, the impact of opioids on transplant recipients remains poorly studied. The purpose of this study was to investigate the impact of a protocol that eliminated routine PCA use and implemented aggressive multimodal post-operative pain control in renal transplant recipients. The notable findings were threefold: 1) multimodal analgesia increased significantly following implementation of a formal post-operative pain control protocol; 2) PCA use decreased significantly; 3) patients with and without a PCA who required minimal opioids on the day prior to discharge were prescribed a disproportionate amount of opioids at the time of discharge.

The transplant community has been largely impacted by the opioid epidemic because the number of deceased donors has increased dramatically in the setting of more opioid overdoses.[7] More recently, however, investigation has turned towards the impact of opioids on transplant recipients, as research has repeatedly demonstrated the perils of opioid-based pain control after surgical procedures in a variety of different populations.[1,6] Other authors have focused on the relationship between pre-transplant opioid usage and the increased risk for post-transplant opioid addiction, graft failure, and death.[2,8,9]

Establishing accurate expectations regarding post-operative pain has proven essential in other studies of opioid reduction.[10,11] However, this was challenging in our patient

population for several reasons. First, all transplant recipients in our program are counseled extensively prior to transplant, but the majority of our renal transplant recipients receive deceased donor grafts and typically spend 8–10 years on our waiting list. As a result, their most recent interaction with the outpatient pre-transplant providers could have occurred many months prior to their transplant admission and therefore left little room for counseling regarding post-operative pain control. Second, while we worked extensively to educate the inpatient providers, we did not engage the outpatient providers with the same vigor. As a result, patients admitted for transplant who had recently been seen in the transplant clinic came in with the expectation that they would receive a button to control their pain after the transplant.

Flyers were widely distributed and posted on the transplant floor at the start of the study, to ensure all providers were aware of the new protocol. However, we could have better communicated the ultimate goal of the intervention, which was to decrease opioid prescriptions at discharge. Furthermore, we did not maintain ongoing communication with providers after the start of the study. Other groups have successfully relayed the purpose of their efforts by disseminating guidelines and giving presentations throughout the study period to their providers.[6,12]

We did not see a decrease in the amount of inpatient or discharge opioids prescribed in patients who did not receive PCA analgesia. Most notably, patients with and without a PCA who required minimal opioids on the day prior to discharge were prescribed more opioids at discharge than recommended, in both the pre- and post-intervention eras. We believe that the lack of protocolization of opioids prescribed at discharge played a role in this finding. While we implemented a specific intervention to eliminate inpatient PCA use, we did not extend the protocol to regulate the amount of opioids to be prescribed at discharge. Recent legislative efforts to quantify discharge medications, such as the "7-day supply"[6] may be too imprecise and may have a deleterious effect on opioid reduction protocols.

In a meta-analysis of interventions for postsurgical opioid prescribing that encompassed eight studies, Wetzel et al found that direct methods in the form of organizational interventions were more effective than indirect, clinician-mediated interventions.[13] Following this present study and the finding that patients were prescribed excessive amounts of opioids at discharge regardless of their inpatient opioid requirements, we initiated a new protocol wherein all patients, regardless of how many opioids received while inpatient, receive 10 opioid pills at discharge. Patients with a history of chronic pain pre-operatively will be excluded. We plan to analyze the number of refills needed, to evaluate whether this opioid-sparing approach at discharge leads to sufficient pain control in the short post-operative term.

This study highlights the importance of communication. Transplantation is a true multidisciplinary endeavor that involves extensive pre-transplant evaluation, intense care during the transplant hospitalization, and long-term follow-up with the transplant program. As a result, there are an enormous number of providers involved in just a single patient's care. Better communication with the outpatient services, and additional education for the

inpatient providers on the individual nature of discharge opioid requirements would have added substantially to this protocol.

There are several limitations to this study. First, the data is from a single transplant center and therefore the findings may be limited in their generalizability. The small sample size could have led to a type II error. However, the single center data enabled a detailed review of patient medications, which is not possible with large database research. Second, this was not a randomized study and we, therefore, cannot claim a causal relationship between PCA elimination and opioid reduction or increased use of non-opioid analgesics. Despite these limitations, we think this study demonstrates the importance of a collaborative approach to opioid reduction and highlights the need for providers to continually work to decrease opioid use in the inpatient setting and at discharge.

Conclusions

The introduction of a protocol that eliminated PCA usage and added non-opioid adjunct medications significantly increased the use of non-opioid adjuncts in renal transplant recipients. Patients continued to be prescribed excess opioids at discharge compared to inpatient opioid use the day prior to discharge. Ongoing communication with all providers caring for renal transplant recipients and protocolization of the different stages of a patient's post-operative hospitalization are crucial. Providers should continue to question the status quo with regards to pain management policies and continue working to minimize opioid use in surgical patients.

Acknowledgments

Appendix 1. Opioid reduction protocol

- Providers writing post-operative orders
    - Scheduled PO Acetaminophen 1000 mg q8h
    - Gabapentin 300mg PO qhs (for 7 days)
    - Lidoderm patch PRN moderate pain
    - PO Oxycodone 5–10 mg q4h prn severe pain
    - IV Dilaudid 0.4 mg q3h prn breakthrough pain
    - No Toradol
- Providers writing orders on the ward:

– If pain not controlled: ok for IV Dilaudid 0.4 mg breakthrough dose x2 prn

– If requires additional narcotic after breakthrough dosing, change frequency to IV Dilaudid 0.4 mg q2h prn

– If pain still not controlled, increase dosing to IV Dilaudid 0.6 mg q2h prn

– If pain still not controlled, start PCA

– Timing of transition to PO medications will be the same (when advanced to diet, typically on POD1)

♦ Scheduled PO Acetaminophen 1000 mg q8h

♦ PO Oxycodone 5–10 mg q4h prn severe pain

♦ IV Dilaudid 0.4 mg q4h prn severe pain not controlled by Oxycodone

References

1. Brummett CM, Waljee JF, Goesling J, et al. New Persistent Opioid Use After Minor and Major Surgical Procedures in US Adults. JAMA Surg. 2017;152(6):e170504. 10.1001/jamasurg.2017.0504 [PubMed: 28403427]

2. Abbott KC, Fwu CW, Eggers PW, et al. Opioid Prescription, Morbidity, and Mortality in US Transplant Recipients. Transplantation. 2018;102(6):994–1004. 10.1097/TP.0000000000002057 [PubMed: 29319627]

3. Morlion B, Schafer M, Betteridge N, Kalso E. Non-invasive patient-controlled analgesia in the management of acute postoperative pain in the hospital setting. Curr Med Res Opin. 2018;34(7):1179–1186. 10.1080/03007995.2018.1462785 [PubMed: 29625532]

4. Hudcova J, McNicol E, Quah C, et al. Patient controlled opioid analgesia versus conventional opioid analgesia for postoperative pain. The Cochrane database of systematic reviews. 2006(4):CD003348. [PubMed: 17054167]

5. Sun EC, Darnall BD, Baker LC, Mackey S. Incidence of and Risk Factors for Chronic Opioid Use Among Opioid-Naive Patients in the Postoperative Period. JAMA Intern Med. 2016;176(9):1286–1293. 10.1001/jamainternmed.2016.3298 [PubMed: 27400458]

6. Hill MV, Stucke RS, Billmeier SE, et al. Guideline for Discharge Opioid Prescriptions after Inpatient General Surgical Procedures. J Am Coll Surg. 2018;226(6):996–1003. 10.1016/j.jamcollsurg.2017.10.012 [PubMed: 29198638]

7. Durand CM, Bowring MG, Thomas AG, et al. The Drug Overdose Epidemic and Deceased-Donor Transplantation in the United States: A National Registry Study. Ann Intern Med. 2018;168(10):702–711. 10.7326/M17-2451 [PubMed: 29710288]

8. Randall HB, Alhamad T, Schnitzler MA, et al. Survival implications of opioid use before and after liver transplantation. Liver Transpl. 2017;23(3):305–314. 10.1002/lt.24714 [PubMed: 28027603]

9. Lentine KL, Lam NN, Naik AS, et al. Prescription opioid use before and after kidney transplant: Implications for posttransplant outcomes. Am J Transplant. 2018;18(12):2987–2999. 10.1111/ajt.15565 [PubMed: 29498196]

10. Holman JE, Stoddard GJ, Horwitz DS, Higgins TF. The effect of preoperative counseling on duration of postoperative opiate use in orthopaedic trauma surgery: a surgeon-based comparative cohort study. J Orthop Trauma. 2014;28(9):502–506. 10.1097/BOT.0000000000000085 [PubMed: 24667804]

11. Sugai DY, Deptula PL, Parsa AA, Don Parsa F. The importance of communication in the management of postoperative pain. Hawaii J Med Public Health. 2013;72(6):180–184. [PubMed: 23795326]

12. Howard R, Waljee J, Brummett C, et al. Reduction in Opioid Prescribing Through Evidence-Based Prescribing Guidelines. JAMA Surg. 2018;153(3):285–287. 10.1001/jamasurg.2017.4436 [PubMed: 29214318]

13. Wetzel M, Hockenberry J, Raval MV. Interventions for Postsurgical Opioid Prescribing: A Systematic Review. JAMA Surg. 2018;153(10):948–954. 10.1001/jamasurg.2018.2730 [PubMed: 30140931]

Research Highlights

- The impact of inpatient opioid analgesia post-renal transplant on discharge prescriptions is unknown.

- Most renal transplant recipients are prescribed more opioids at discharge than they would be expected to require based on inpatient opioid use on the day prior to discharge.

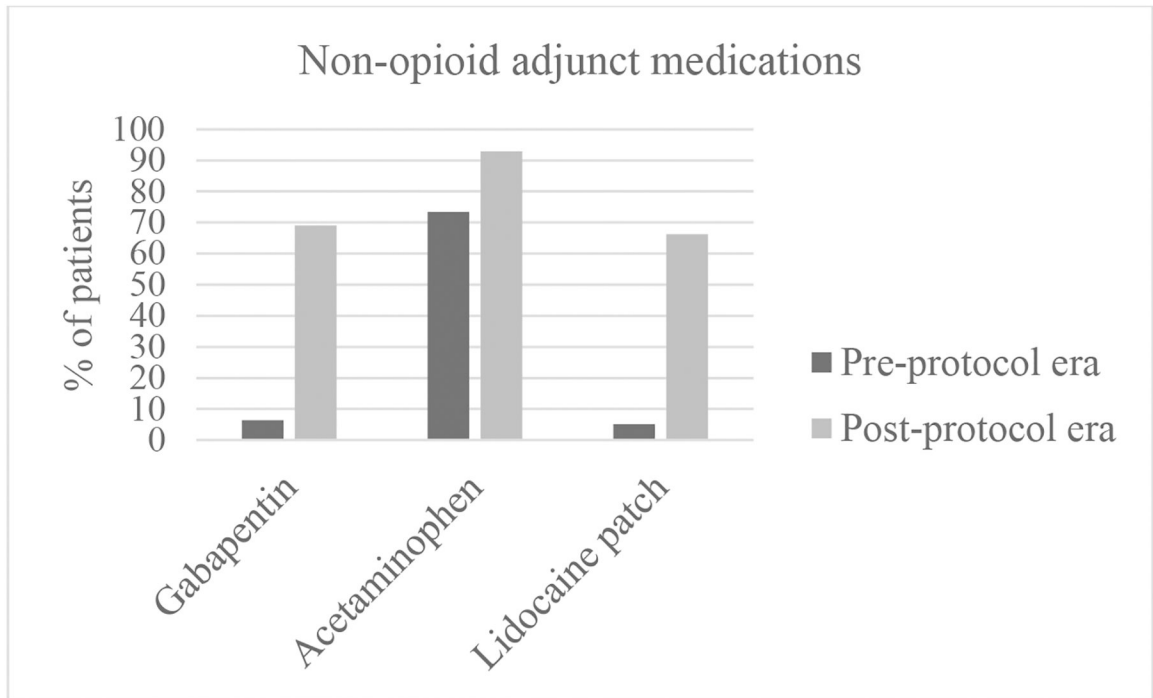- Multimodal analgesia significantly increased following a formal opioid-reduction protocol.

Figure 1.
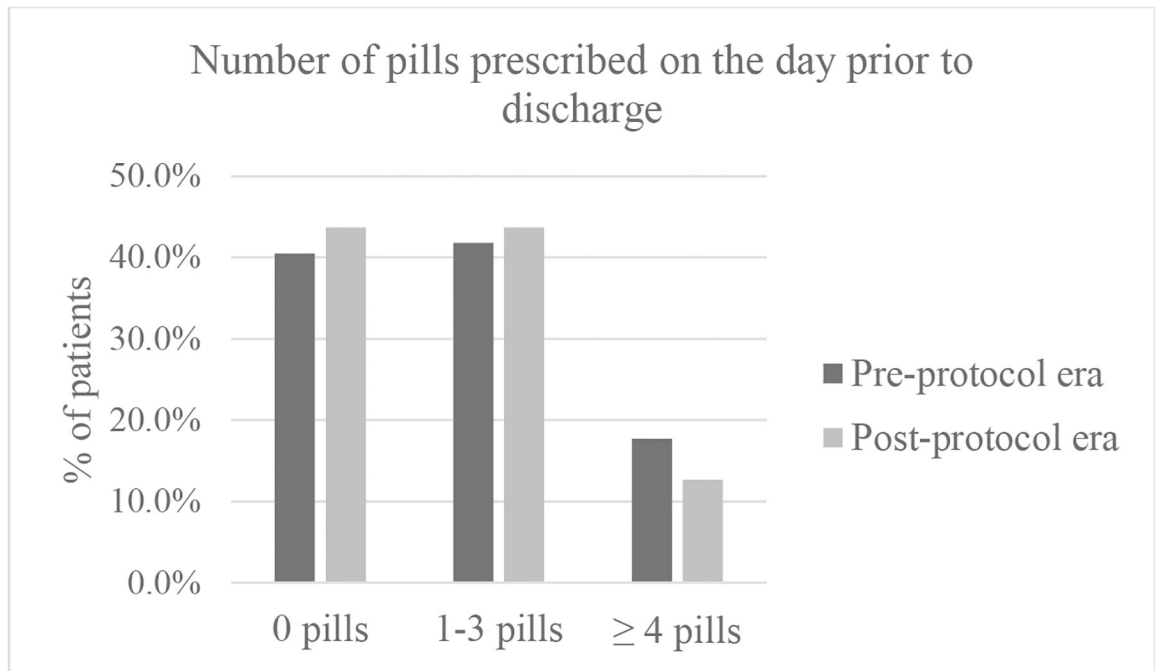Non-opioid adjunct medications pre-protocol and post-protocol introduction.

Figure 2.
Opioids prescribed (as number of pills) on the day prior to discharge, in the pre-protocol and post-protocol eras.
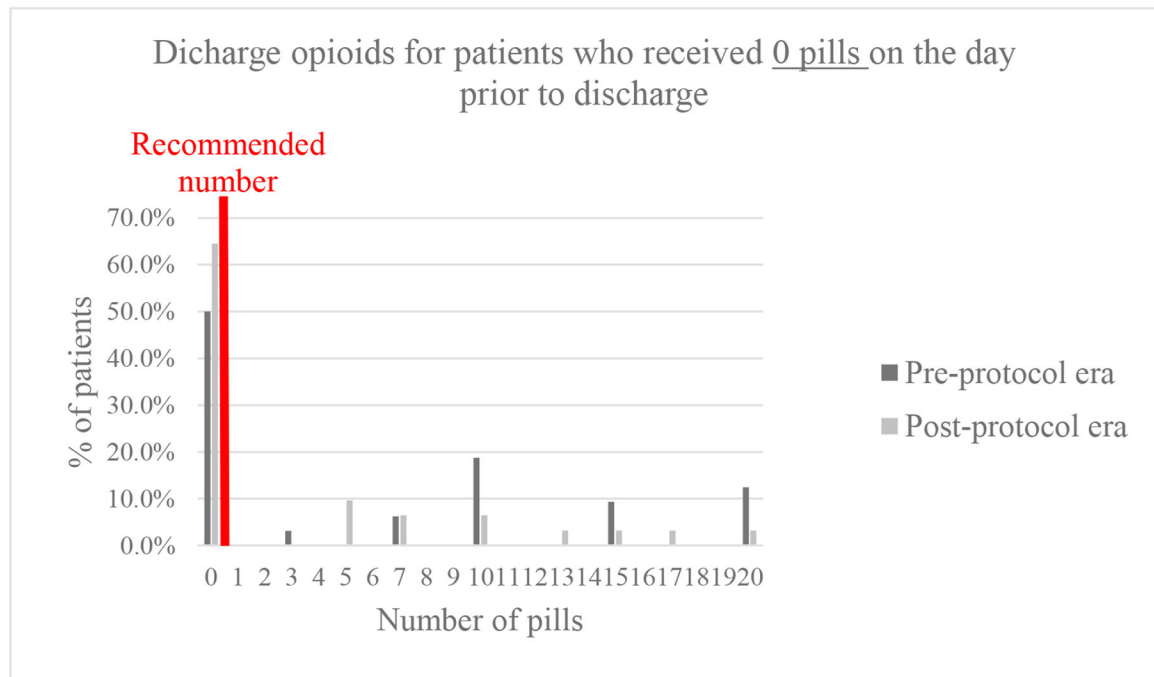
Figure 3.
Opioids prescribed (as number of pills) at discharge during the Pre-protocol and Post-protocol eras in Group A patients who received 0 opioid pills on the day prior to discharge. The red bar indicates the recommended number of pills to be prescribed at discharge for this patient group.[6]

Figure 4.
Opioids prescribed (as number of pills) at discharge during the Pre-protocol and Post-protocol eras in Group B patients who received 1–3 opioid pills on the day prior to discharge. The red bar indicates the recommended number of pills to be prescribed at discharge for this patient group.[6]
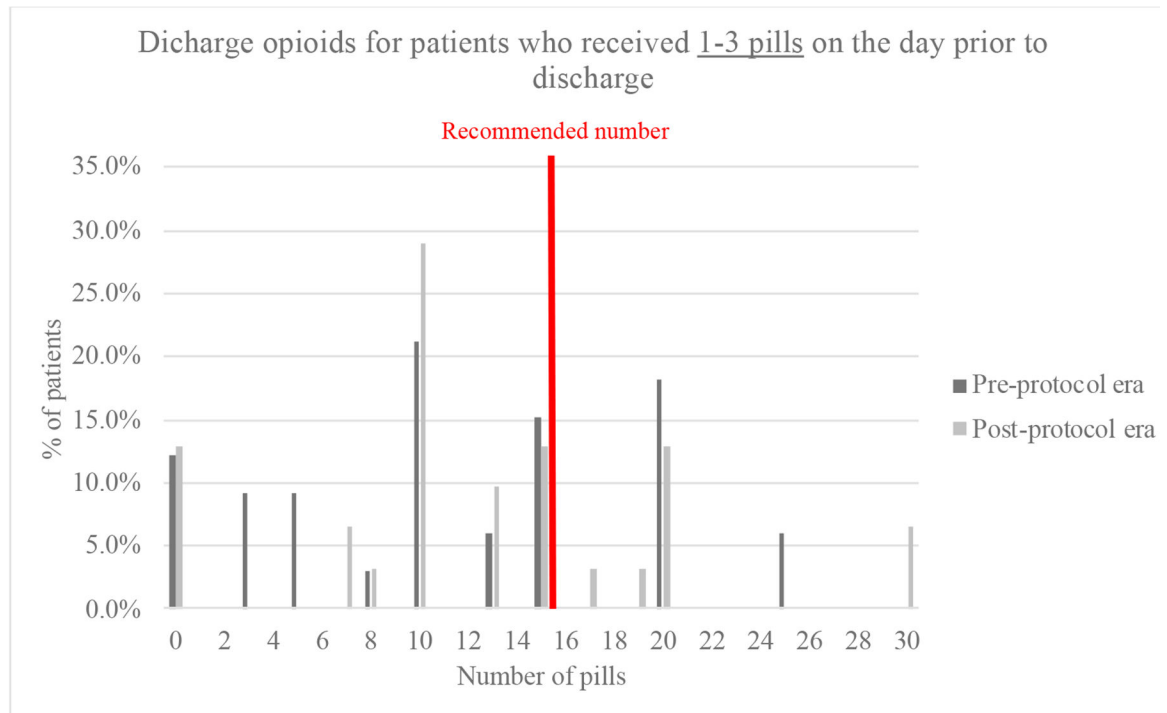
Figure 5.
Opioids prescribed (as number of pills) at discharge during the Pre-protocol and Post-protocol eras in Group C patients who received 4 opioid pills on the day prior to discharge. The red bar indicates the recommended number of pills to be prescribed at discharge for this patient group.[6]
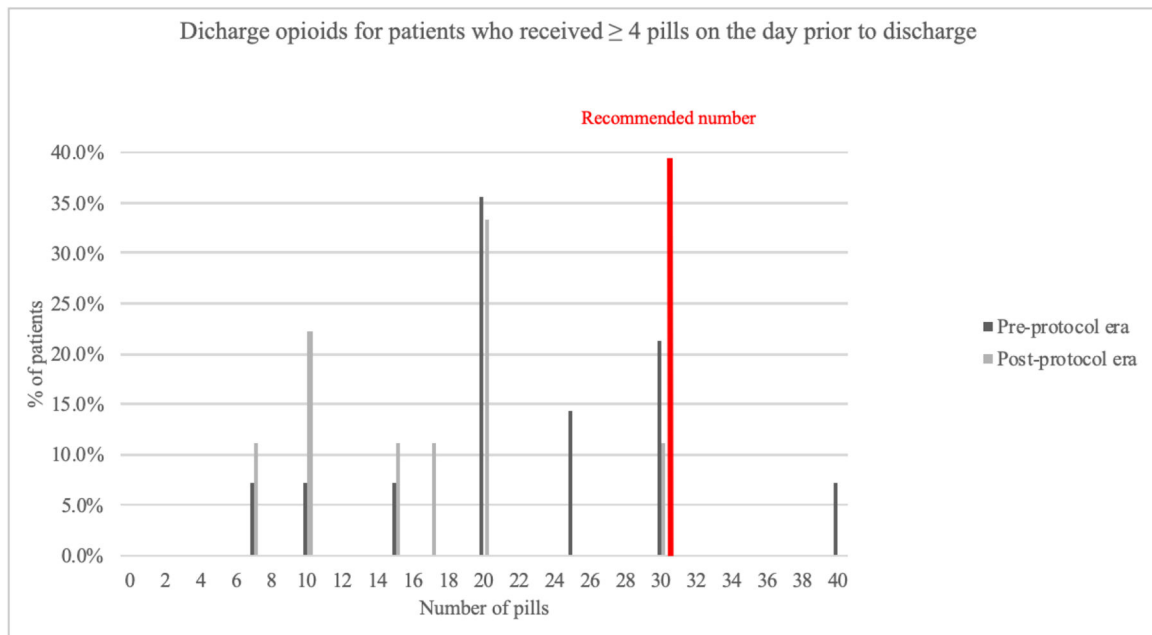
Table 1.

Patient demographics

	Pre-protocol (n=79)	Post-protocol (n=71)	p-value
Age, median (range)	51 (22–80)	56 (20–80)	0.06
Female sex, % (n)	46.8% (37)	50.7% (36)	0.76
Race/Ethnicity, % (n)			0.03
African American	12.7% (10)	12.7% (9)	
American Indian/Alaska Native	0	1.4% (1)	
Asian	30.4% (24)	22.5% (16)	
Hispanic	12.7% (10)	23.9% (17)	
Pacific Islander	0	2 (1.3%)	
White	19% (15)	28.2% (20)	
Unknown	25.3% (20)	8.5% (6)	
ESRD etiology, % (n)			0.002
Type 2 DM	19 (24.1%)	24 (33.8%)	
Hypertension	13 (16.5%)	15 (21.1%)	
Primary GN	23 (29.1%)	4 (5.6%)	
Secondary GN	9 (11.4%)	9 (12.7%)	
Interstitial	1 (1.3%)	2 (2.8%)	
Congenital/Genetic	3 (3.8%)	11 (15.5%)	
Other	11 (13.9%)	6 (8.5%)	