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ARTICLE

The impact of regional anesthesia on opioid demand in distal radius fracture surgery

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ABSTRACT

Purpose: Regional anesthesia (RA) is commonly used in distal radius fracture surgery to reduce pain and opioid consumption. The purpose of this study was to evaluate the real-world impact of RA on inpatient and outpatient opioid consumption and demand in patients undergoing distal radius fracture surgery.

Methods: All patients ages 18 and older undergoing distal radius fracture surgery between 7/2013 and 7/2018 at a single institution ($n = 969$) were identified. Inpatient opioid consumption and outpatient opioid prescribing in oxycodone 5-mg equivalents (OE's) up to 90-d post-operative were recorded for patients with and without RA. Adjusted models were used to evaluate the impact of RA on opioid outcomes.

Results: Adjusted models demonstrated decreases in inpatient opioid consumption in patients with RA (10.7 estimated OE's without RA *vs.* 7.6 OE's with RA from 0 to 24 h post-op, 10.2 *vs.* 5.3 from 24 to 48 h post-op and 7.5 *vs.* 5.0 from 48 to 72 h post-op, $p < .05$). Estimated cumulative outpatient opioid demand was significantly higher in patients with RA (65.3 OE's without RA *vs.* 81.0 with RA from 1-month pre-op to 2-week post-discharge, 76.1 *vs.* 87.7 OE's to 6-weeks, and 80.8 *vs.* 93.5 OE's to 90-d, all p values for RA $< .05$) though rates of refill were significantly lower in patients with RA from 2-week to 6-week post-op compared to patients without RA.

Conclusions: Patients undergoing RA in distal radius fracture surgery had decreased inpatient opioid consumption but increased outpatient demand after adjustment for patient and operative characteristics.

Level of evidence: Level III, retrospective, therapeutic cohort study.

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KEYWORDS
Distal radius fracture; regional anesthesia; opioid

Introduction

The opioid epidemic has become a major public health concern in recent decades with recognition of the problem reaching far beyond the medical community. However, despite increased awareness and appropriate institutional, state and federal legislative efforts to reduce opioid misuse, opioid deaths have continued to rise [1–9]. As some of the highest prescribers of opioid medications, this issue is of particular concern to orthopaedic providers [4,10]. As such, increased focus has been placed on alternative and adjunctive methods of pain management including local regional anesthesia (RA) such as neuraxial anesthesia and peripheral nerve blocks [11]. The use of RA has been demonstrated to reduce acute post-operative pain after orthopaedic surgery [12–14]. The effect of RA on both chronic post-operative pain as well as long-term opioid use is less well-studied. The studies that do exist have demonstrated mixed effects [15–21].

Distal radius fractures are one of the most commonly encountered fractures and RA is frequently used during operative treatment [22]. Moreover, the incidence of distal radius fractures is on the rise worldwide [23–25]. While prognosis after distal radius fracture is overall favorable, continued pain and disability up to a year after injury is not uncommon [26]. While distal radius fractures are particularly common in the elderly, a high-risk group for the negative outcomes of opioid medications, little research has evaluated the risk of chronic opioid use or the effect of RA in reducing opioid misuse after these fractures. Additionally, the effect of RA on opioid use after distal radius fracture in the perioperative period has been mixed [27–32].

Given this knowledge gap regarding the impact of RA on longitudinal perioperative and post-operative opioid demand, the purpose of this study is to evaluate the impact of these modalities on inpatient opioid consumption and outpatient opioid demand in patients undergoing distal radius fracture surgery. The study hypothesis is that regional anesthesia will be associated with a decrease in inpatient opioid consumption but will not change outpatient opioid demand.

Methods

Study design

This study evaluates inpatient opioid consumption and outpatient opioid demand in all patients ages 18 and older undergoing distal radius fracture surgery over a 5-year period at a single institution (7/2013 – 7/2018). This retrospective, observational cohort study was designed and reported in accordance with the STROBE statement on reporting observational studies [33]. The institutional review board reviewed and approved this study.

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Variables and data sources

Patients were identified as undergoing distal radius fracture surgery by Current Procedural Terminology (CPT) codes 25607, 25608 and 25609. Chart review was used to extract information on RA, age, sex, race, body mass index (BMI), smoking status, American Society of Anesthesiologists (ASA) score, injury mechanism, additional injuries, open fracture and additional surgery. Patients with one or more opioid prescriptions within the 6-month to 1-month pre-operative time period were considered to have had pre-operative opioid usage and possible dependence. This aligns with the Centers for Disease Control (CDC) definition [34]. Outcomes included daily (0–24, 24–48 and 48–72 h post-op) inpatient opioid consumption and outpatient opioid demand (1-month pre-operative to 2-weeks post-operative, 6-weeks post-operative and 90-d post-operative) in terms of oxycodone 5-mg equivalents (OE's) based on conversion factors provided by the CDC [35]. The 1-month pre-operative timeframe was included since many patients had delayed treatment of their fractures after initial splinting. Counts and rates of outpatient prescriptions and refills were also tabulated. For further characterization of the study population, 90-d mortality, surgical site infection, compartment syndrome, loss of fixation, deep vein thrombosis (DVT), pulmonary embolism (PE), falls, delirium and ileus.

As shown in Table 1, patients without RA tended to be males with higher BMI and had higher rates of elevated ASA score, high energy injury, additional injury and additional surgery. Most RA was performed as a single-shot block ($n = 763$, 88.3%). Supraclavicular ($n = 643$, 74.4%), infraclavicular ($n = 151$, 17.5%) and axillary ($n = 35$, 4.1%) were most common. Medial brachial, interscalene, median, musculocutaneous, radial, retroclavicular, subclavian and suprascapular blocks were each utilized <2% of cases.

Pain protocol

RA is commonly used by anesthesiologists at our institution, and the decision for RA is made on a case-by-case basis. Surgeons routinely use post-operative multimodal analgesia including acetaminophen and oral and intravenous (IV) opioids. Oral opioids (oxycodone and hydrocodone) are administered on an as-needed basis according to a visual analog scale (VAS) for pain (generally 5–15 mg oxycodone every 4 h as needed for pain). Patient-controlled analgesia (PCA) with hydromorphone or morphine is sometimes used, particularly for patients with pain that is difficult to control with oral medications. Additional as-needed IV opioids (commonly hydromorphone) is utilized for breakthrough pain. Adjunctive oral and IV non-steroidal anti-inflammatory pain medications (NSAID's) are not frequently used after distal radius fracture surgery at our institution. Discharge pain medications are not standardized, but 822 of 969 (84.8%) of patients in this series received a discharge opioid prescription.

Missing data

There were 41 of 1010 (4.1%) of patients whose BMI could not be determined. Overall results were evaluated with and without

Table 1. Baseline patient, injury, and treatment characteristics for patients with and without RA. Proportions (percentages) and medians (Q1, Q3) displayed.

Factors	Without RA ($n = 105$)	With RA ($n = 864$)	p Value
Age (years)	54.9 (38.5, 66.2)	59 (46.6, 68.5)	.059
Female sex	64/105 (61%)	630/864 (72.9%)	.012
Caucasian race	71/105 (67.6%)	660/864 (76.4%)	.055
BMI (kg/m^2)	28.2 (24.1, 33.1)	26.6 (23.3, 31)	.042
Smoking	16/101 (15.8%)	121/848 (14.3%)	.34
Pre-operative opioid usage	6/105 (5.7%)	78/864 (9%)	.36
ASA score			
ASA 3 or greater	45/103 (43.7%)	268/854 (31.4%)	.026
ASA 1	8/105 (7.6%)	129/864 (14.9%)	.052
ASA 2	50/105 (47.6%)	457/864 (52.9%)	.35
ASA 3	41/105 (39%)	239/864 (27.7%)	.017
ASA 4	4/105 (3.8%)	29/864 (3.4%)	.77
ASA not documented	2/105 (1.9%)	10/864 (1.2%)	.38
Injury mechanism			
High energy mechanism	57/101 (56.4%)	217/796 (27.3%)	<.001
High energy mechanism			
Crush injury	1/105 (1%)	3/864 (0.3%)	.37
Fall from height	23/105 (21.9%)	119/864 (13.8%)	.039
GSW	0/105 (0%)	1/864 (0.1%)	1
MVC	32/105 (30.5%)	91/864 (10.5%)	<.001
MVC *vs.* ped	1/105 (1%)	3/864 (0.3%)	.37
Low energy mechanism			
Assault	0/105 (0%)	2/864 (0.2%)	1
Ground level fall	44/105 (41.9%)	562/864 (65%)	<.001
Sporting injury	0/105 (0%)	15/864 (1.7%)	.39
Unknown energy mechanism			
Not documented	4/105 (3.8%)	62/864 (7.2%)	.3
Other	0/105 (0%)	6/864 (0.7%)	1
Additional injury	55/105 (52.4%)	179/864 (20.7%)	<.001
Open fracture	8/105 (7.6%)	30/864 (3.5%)	.056
Additional surgery within 7 d	10/105 (9.5%)	2/864 (0.2%)	<.001
Additional surgery within 90 d	16/105 (15.2%)	22/864 (2.5%)	<.001
RA characteristics			
RA route continuous	0/105 (0%)	87/864 (10.1%)	n/a
RA route multiple	0/105 (0%)	1/864 (0.1%)	n/a
RA route not documented	0/105 (0%)	13/864 (1.5%)	n/a
RA route single shot	0/105 (0%)	763/864 (88.3%)	n/a
RA (number)	0 (0, 0)	1 (1, 1)	n/a

p Values from Fisher's exact test or Wilcoxon rank-sum. Red coloring highlights statistical significance.

these patients and found to be similar. In order to adjust for the potential impact of this characteristic, these patients were excluded from the multivariable analyses leaving 969 patients for analysis.

Statistical analysis

Descriptive statistics including proportions with percentages for categorical data or medians with quartiles for continuous data were calculated as appropriate for patients with and without RA. Unadjusted differences in outcomes between these two cohorts were evaluated with Fisher's exact test for categorical outcomes and Wilcoxon rank-sum for continuous outcomes (inpatient opioid consumption and outpatient prescription volume). To adjust for the impact of baseline patient and treatment characteristics, multivariable modeling was planned. Positive skew was anticipated for the study's opioid demand outcomes since they were count data. After confirming non-normal distribution through data visualization with histograms and Shapiro–Wilks testing, we elected to model outcomes with a generalized linear model utilizing the negative binomial distribution and log link function. We also excluded the top 2% of opioid utilizers due to their outlier status. Further, since treatment was not randomly assigned, we chose to include propensity score weighting in the statistical analysis. Both the propensity score weighting and generalized linear models included age, sex, race, BMI, smoking, pre-op opioid usage, ASA score (binarized to 1–2 *vs.* 3 or more), injury energy (binarized to high *vs.* low energy), presence of additional injuries, open injury and additional surgery within 7-d post-fracture surgery as model covariates. In this way, analyses were performed in a 'doubly robust' fashion [36,37]. This generalized linear modeling provided incident rate ratios to describe the impact of RA on outcomes. In order to help readers better understand the real-world, adjusted impact of RA on outcomes, treatment *vs.* no treatment was simulated in each patient within the dataset. Effect estimates derived from the medians of the point estimates and 95% confidence intervals were generated. Additionally, histograms displaying the simulated treatment *vs.* no treatment population were also produced. R and R Studio (R: A Language and Environment for Statistical Computing, R Core Team, R Foundation for Statistical Computing, Vienna, Austria, 2020) were used for statistical calculations. *p* Values less than .05 were considered significant.

Results

RA was associated with significantly decreased inpatient opioid demand up to 72 h post-operative after adjusting for baseline treatment and operative characteristics (Table 2 and Figure 1(a–c)). However, when adjusting for baseline patient and treatment characteristics, there was a significant association of RA with increased outpatient opioid demand up to 90-d post-operative (Table 3 and Figure 2(a–c)). Nonetheless, the difference in magnitude of prescribing between groups was similar to the difference in volume that had been prescribed in the 1-month pre-operative time period between groups (approximately 13.3 oxycodone 5-mg equivalents). When adjusting for baseline patient and treatment characteristics, early refill (discharge to 2-weeks post-operative were significantly higher in patients with RA. However, rates of 2-week to 6-week filling were significantly lower in patients with RA (Table 4). General 90-d outcomes did not differ significantly between groups in unadjusted and adjusted analyses (Table 5).

Appendix Tables 1–3 display complete results of multivariable modeling. For inpatient opioid consumption, adjusted models demonstrated significant increases in consumption with Caucasian race, increased BMI, smoking, high-energy mechanism, additional injury and decreases in consumption with increased age, additional surgery, and RA (Appendix Table 1). For outpatient opioid prescribing, adjusted models demonstrated significant increases in demand with increased BMI, smoking, pre-operative opioid usage, high-energy mechanism, additional injury, and RA but decreases with increased age and increased ASA (Appendix Table 2). Odds of opioid fill or refill were significantly decreased with increased age, increased ASA and RA (2–6 weeks) while it was significantly increased with Caucasian race, smoking, high-energy mechanism and RA (discharge to 2 weeks).

Appendix Tables 4–6 demonstrate the unadjusted inpatient opioid consumption and outpatient opioid demand metrics and largely align with the adjusted findings. Patients with RA consumed significantly lower volume of opioids while inpatient at all timepoints up to 72-h post-operative. Outpatient opioid demand did not differ significantly in patients with and without RA up to 90-d post-operative. However, patients with RA requested fewer refills from 2-weeks to 90-d post-operative.

Discussion

In this study of perioperative opioid demand in patients undergoing fixation of distal radius fractures with and without RA, there were decreases in inpatient opioid consumption and mixed effects on outpatient opioid demand after adjusting for baseline patient characteristics. Age, race, BMI, smoking, pre-operative opioid usage, injury energy and additional surgery/injuries were significant drivers of inpatient and outpatient opioid demand metrics.

This study found significant reductions in inpatient opioid use up to 72 h post-op after RA compared to patients who did not receive a nerve block. Previous research on inpatient opioid use after distal radius fracture has produced differing results. A 2016 randomized controlled trial found that while opioid use in the first 24 h was reduced for those who were given a brachial plexus blockade, these patients reported worse pain than the general anesthesia group 12–24 h after surgery [28]. Similarly, Rundgren et al. found that patients who received RA had reduced opioid consumption in the first 24 h after surgery; however, these patients had increased opioid utilization from 24 to 72 h after surgery and no significant difference in opioid consumption when looking at the time period as a whole [30]. Wong et al. found a reduction in morphine use in the post-operative care unit, but no difference in oral analgesic consumption up to 48 h after surgery [38].

It has been argued that the immediate reduction in opioid use after RA and subsequent comparative or even increased opioid use at the 1–2-d post-operative mark is a result of 'rebound pain'

Table 2. Adjusted inpatient oxycodone 5-mg equivalents consumed in patients with and without RA. Red coloring highlights statistical significance.

Timeframe	Oxycodone without RA (95% CI)	Oxycodone with RA (95% CI)	Incident rate ratios (95% CI, *p* value)
0–24 h post-op	10.7 (7.3, 15.5)	7.6 (5.2, 11)	0.71 (0.59, 0.86; $p = <.001$)
24–48 h post-op	10.2 (6.5, 14.6)	5.3 (3.4, 7.7)	0.52 (0.42, 0.64; $p = <.001$)
48–72 h post-op	7.5 (4.4, 12.5)	5 (2.9, 8.3)	0.67 (0.5, 0.89; $p = .005$)

Simulated estimates from multivariable model (95% CI) displayed. Incident rate ratios and *p* values from multivariable model.

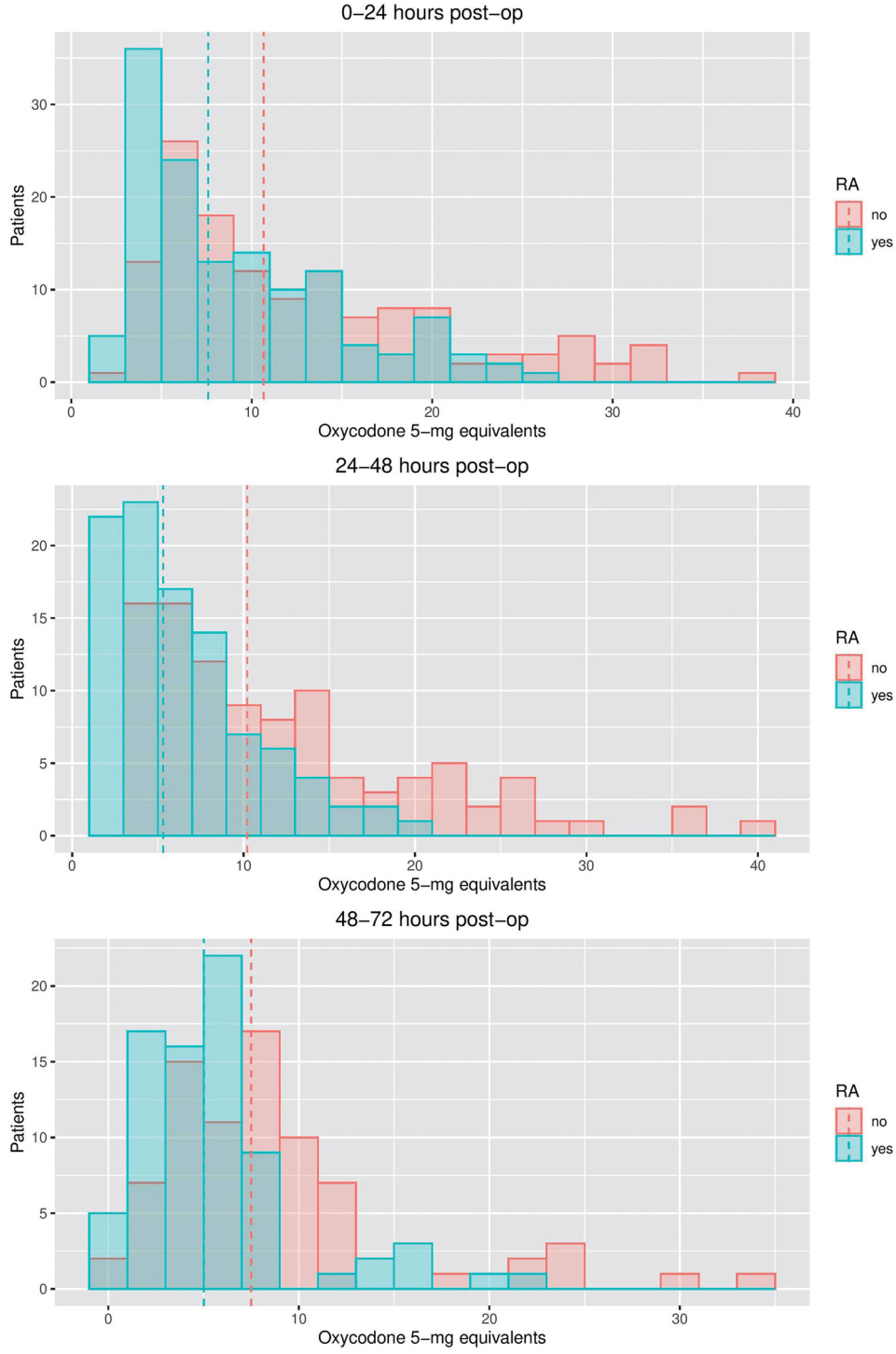

Figure 1. (a–c) Predicted inpatient opioid consumption histogram in oxycodone 5-mg equivalents in patients with (green) and without (red) RA from 0 to 72 h post-operative. Vertical bars represent mean consumption.

Table 3. Adjusted outpatient oxycodone 5-mg equivalents prescribed in patients with and without RA. Red coloring highlights statistical significance.

Timeframe	Oxycodone without RA (95% CI)	Oxycodone with RA (95% CI)	Incident rate ratios (95% CI, *p* value)
1 month pre-op to 2 weeks	65.3 (56.9, 75.3)	81 (70.5, 93.4)	1.24 (1.14, 1.35; $p = <.001$)
1 month pre-op to 6 weeks	76.1 (66.2, 88)	87.7 (76.2, 101.4)	1.15 (1.05, 1.26; $p = .001$)
1 month pre-op to 90 d	80.8 (70.5, 93.9)	93.5 (81.4, 108.6)	1.16 (1.06, 1.27; $p = .001$)

Simulated estimates from multivariable model (95% CI) displayed. Incident rate ratios and *p* values from multivariable model.

after the effects of peripheral nerve blockade wear off. With successful pain control from the block, patients do not take adjuncts or oral opioids early enough. As a consequence, they experience seemingly sudden and increased high levels of pain and subsequently consume more opioids. Wong et al. added scheduled paracetamol to their pain control regimen and demonstrated no rebound pain or increased opioid consumption in patients who received RA [38]. Given that the typical pain regimen at our

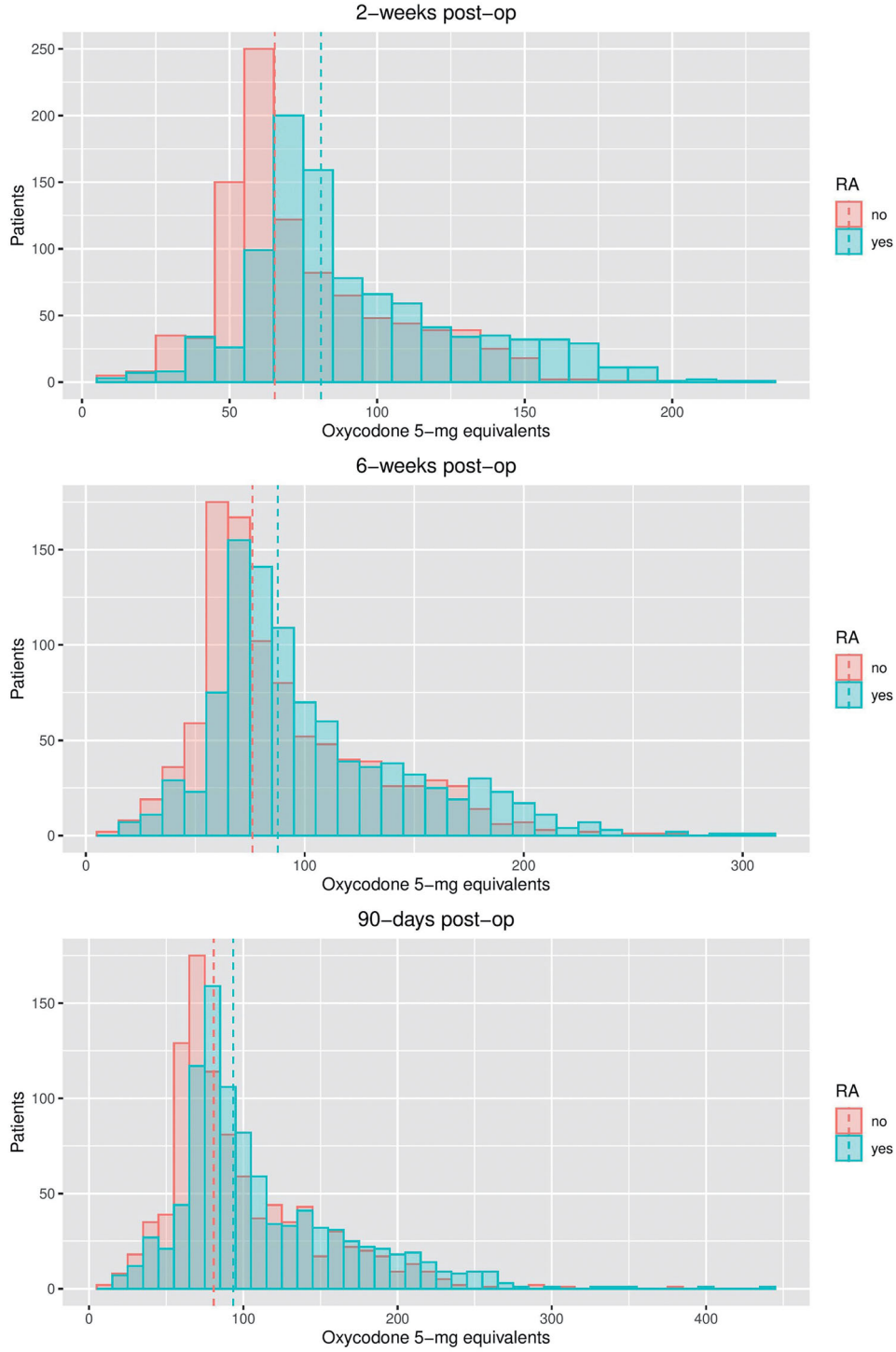

Figure 2. (a–c) Predicted outpatient opioid prescription histogram in oxycodone 5-mg equivalents in patients with (green) and without (red) RA. Vertical bars represent mean prescription.

Table 4. Adjusted odds of opioid fill and refill. Odds ratio (95% CI) displayed.

Factors	Discharge to two-week opioid refill	Two weeks to six weeks opioid fill	Six weeks to ninety-day opioid fill
RA	1.39 (1.1, 1.75; $p = .005$)	0.59 (0.46, 0.74; $p = <.001$)	0.9 (0.68, 1.2; $p = 0.47$)

p values from multivariable modeling. Complete model displayed in Appendix.

institution includes scheduled acetaminophen as well, it is possible that its administration prevented the development of rebound pain and contributed to the sustained reduction in inpatient opioid use. Additionally, this study's sample size of almost 1000 patients was significantly larger than any of the aforementioned studies, the largest of which had a sample size of less than 100.

Interestingly, our study demonstrated increased rates of outpatient opioid demand up to 90 d after surgery as well as an increased likelihood of need for refill within 2 weeks after surgery

Table 5. General 90-d perioperative complications.

Outcomes	All subjects ($n = 969$)	Without RA ($n = 105$)	With RA ($n = 864$)	p Value
Mortality	4/969 (0.4%)	1/105 (1%)	3/864 (0.3%)	.37
SSI	10/969 (1%)	0/105 (0%)	10/864 (1.2%)	.61
Mechanical failure	2/969 (0.2%)	0/105 (0%)	2/864 (0.2%)	1
DVT	2/969 (0.2%)	1/105 (1%)	1/864 (0.1%)	.21
PE	1/969 (0.1%)	1/105 (1%)	0/864 (0%)	.108
ACS	0/969 (0%)	0/105 (0%)	0/864 (0%)	n/c
Falls	14/969 (1.4%)	1/105 (1%)	13/864 (1.5%)	1
Delirium	2/969 (0.2%)	1/105 (1%)	1/864 (0.1%)	.21
Ileus	1/969 (0.1%)	0/105 (0%)	1/864 (0.1%)	1

Proportions (percentages displayed). Unadjusted p values from Fisher's exact test. 'N/c' = not calculable due to low event rate.

for patients who received RA. It is possible that compared to patients who received scheduled acetaminophen inpatient, patients who go home the same day or have a continuous block are less likely to take adjunctive medications or pre-emptive oral opioids and therefore experience more rebound pain once the nerve block wears off. To our knowledge, one study has evaluated the effect of RA on outpatient opioid consumption after distal radius fracture beyond several days post-operative. A 2017 study by O'Neil et al. found no difference in outpatient opioid consumption between patients who received general anesthesia and RA; the longest post-operative usage in their cohort was for 16 d [29]. RA for other orthopaedic surgeries has also not been demonstrated to decrease outpatient opioid use long-term. A 2017 study by Mueller et al. showed no difference in post-operative opioid consumption up to a year after shoulder arthroplasty [19]. In the same year, Sun et al. found no difference after total knee arthroplasty [21]. However, it is important to note that we included prescriptions within the 1-month pre-operative time period towards the cumulative perioperative opioid demand. This was done after careful consideration to account for the opioids that these patients already have available to them. Nonetheless, this is a source of bias against RA. However, this would not likely impact the increased rate of early refill that was seen in this study with RA. Another factor that may have contributed to increased outpatient opioid demand was the higher rate of pre-operative opioid usage (6–1-month pre-operative opioid usage) in patients with RA (9%) compared to no RA (5.7%). While this difference did not reach statistical significance, this factor was included in propensity score weighting and adjusted models in order to account for its impact on opioid demand. Even when accounting for this variable, outpatient opioid demand was increased in patients with RA compared to no RA in terms of volume of opioids prescribed. Rates of refill were higher in patients with RA between discharge and 2-weeks post-operative while rates of refill were lower in patients with RA between 2- and 6-week post-operative. While the rate of pre-operative opioid usage may seem high, it is lower than previously published rates of pre-operative opioid usage in patients undergoing surgery (23%)[39].

While it has been generally hypothesized that RA should help reduce opioid use, research has consistently failed to demonstrate a measurable reduction in prolonged opioid use. However, as demonstrated in prior studies, when combined with medications to help bridge patients as the effects of the nerve block wear off, RA has produced sustained reductions in acute pain. Moreover, acute pain control has been demonstrated to reduce the risk of chronic pain and subsequently prolonged opioid use. Therefore, it stands to reason that RA could have some benefit on prolonged opioid use if more awareness and emphasis is placed on educating patients about adjunctive and pre-emptive oral analgesia even as their pain remains well controlled with RA. More research is needed to evaluate whether preventing rebound pain can produce the hypothesized effects of RA on reducing opioid abuse. Additionally, characterization of the impact of different types (continuous *vs.* single shot), locations and timing (pre-operative or post-operative) of nerve blocks for specific fracture locations could also help improve the success of RA on reducing opioid abuse [40–43]. While this study includes data on these variables, single-shot supraclavicular or infraclavicular nerve blocks were used to a high degree, which limits our ability to detect differences between different locations and routes.

RA has some disadvantages. Nerve blockade often adds time to the perioperative experience for the patient, surgeon and anesthesiologist, incurs additional cost to the healthcare system, and represents an additional procedure for the patient. With these factors in mind, 43% of orthopaedic surgeons do not favor RA due to perceived delays in surgical care and unpredictable clinical results [44].

Study limitations are mainly related to the study's retrospective, observational design. Perioperative multimodal analgesia was not standardized across the institution, so it is possible that there were between-group differences in treatment that could impact opioid utilization. Further, pain was not evaluated as it would not have been collected at standardized intervals, and we would have been unlikely to detect meaningful trends. Further, opioid prescribing rather than opioid consumption was measured in the outpatient setting given the retrospective nature of the study. However, we included information on opioid refills which likely relates well to patient opioid demand. Lastly, our data included patients that received RA at a variety of anatomic locations and with varying medication type, rate, and quantity. Nonetheless, the vast majority of patients underwent a RA utilizing a single-shot supraclavicular or infraclavicular nerve block. While this heterogeneity may decrease the specificity of our results to one particular technique, we believe that analyzing the data in this fashion broadens their clinical interpretation since it more closely matches the scenario encountered in clinical practice.

In conclusion, perioperative RA in distal radius fracture surgery was associated with reduced inpatient opioid consumption but had mixed effects on outpatient opioid demand, which may be related to the increased pre-operative opioid prescribing seen in patients undergoing delayed treatment of distal radius fractures. This information adds depth to patient-physician and physician-physician discussions regarding the utility of perioperative nerve blockade.

Ethical approval

This study was approved by the institutional review board.

Informed consent declaration

This retrospective, observational study did not require informed consent.

Disclosure statement

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. DC and MG conceived the study and obtained ethical approval. DC, ML, TK, EM, SA and AP researched literature and collected data. DC performed data analysis. DC, ML, AP and MG researched literature and wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

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Appendix

Appendix Table 1. Adjusted inpatient opioid usage. Estimates (95% CI) and *p* values from generalized linear model.

Factors	0–24 h post-op	24–48 h oxycodone	48–72 h oxycodone
Age (years)	0.98 (0.98, 0.99; $p=<.001$)	0.98 (0.97, 0.98; $p=<.001$)	0.99 (0.98, 1; $p=.125$)
Female sex	1.08 (0.86, 1.35; $p=.5$)	1.2 (0.93, 1.55; $p=.152$)	1.26 (0.89, 1.78; $p=.184$)
Caucasian race	1.82 (1.46, 2.28; $p=<.001$)	1.59 (1.25, 2.03; $p=<.001$)	1.21 (0.84, 1.73; $p=.31$)
BMI (kg/m^2)	1.01 (1, 1.03; $p=.041$)	1 (0.98, 1.01; $p=.59$)	1 (0.98, 1.02; $p=.81$)
Smoking	1.5 (1.13, 1.99; $p=.005$)	1.82 (1.31, 2.52; $p=<.001$)	2.68 (1.72, 4.16; $p=<.001$)
Pre-operative opioid usage	0.94 (0.67, 1.34; $p=.75$)	0.72 (0.46, 1.12; $p=.142$)	1.01 (0.56, 1.81; $p=.98$)
ASA 3 or greater	1.01 (0.81, 1.25; $p=.95$)	1.27 (1, 1.63; $p=.052$)	0.91 (0.65, 1.26; $p=.56$)
High energy mechanism	2 (1.54, 2.61; $p=<.001$)	1.91 (1.37, 2.66; $p=<.001$)	2.1 (1.3, 3.38; $p=.002$)
Additional injury	1.18 (0.92, 1.51; $p=.197$)	1.08 (0.79, 1.46; $p=.64$)	3.18 (1.6, 6.35; $p=.001$)
Open fracture	1.05 (0.81, 1.36; $p=.71$)	0.89 (0.65, 1.2; $p=.43$)	0.88 (0.56, 1.37; $p=.57$)
Additional surgery within 7 d	0.75 (0.58, 0.96; $p=.025$)	0.83 (0.66, 1.05; $p=.114$)	1.11 (0.84, 1.47; $p=.45$)
RA	0.71 (0.59, 0.86; $p=<.001$)	0.52 (0.42, 0.64; $p=<.001$)	0.67 (0.5, 0.89; $p=.005$)

Appendix Table 2. Adjusted outpatient opioid usage. Estimates (95% CI) and *p* values from generalized linear model.

Factors	1 month pre-op to 2 weeks	1 month pre-op to 6 weeks	1 month pre-op to 90 d
Age (years)	0.99 (0.99, 0.99; $p=<.001$)	0.99 (0.99, 0.99; $p=<.001$)	0.99 (0.99, 1; $p=<.001$)
Female sex	0.95 (0.85, 1.06; $p=.32$)	0.92 (0.82, 1.03; $p=.151$)	0.95 (0.85, 1.07; $p=.41$)
Caucasian race	0.95 (0.85, 1.06; $p=.37$)	1.02 (0.91, 1.14; $p=.74$)	1.05 (0.94, 1.17; $p=.4$)
BMI (kg/m^2)	1.01 (1, 1.02; $p=.011$)	1.01 (1.01, 1.02; $p=<.001$)	1.01 (1.01, 1.02; $p=<.001$)
Smoking	1.11 (0.98, 1.27; $p=.104$)	1.19 (1.05, 1.37; $p=0.008$)	1.19 (1.04, 1.37; $p=.009$)
Pre-operative opioid usage	1.13 (0.97, 1.33; $p=.114$)	1.35 (1.16, 1.58; $p=<0.001$)	1.68 (1.43, 1.97; $p=<.001$)
ASA 3 or greater	0.94 (0.85, 1.05; $p=.29$)	0.91 (0.82, 1.01; $p=.068$)	0.88 (0.79, 0.98; $p=.021$)
High energy mechanism	1.52 (1.35, 1.72; $p=<.001$)	1.51 (1.34, 1.71; $p=<.001$)	1.56 (1.38, 1.78; $p=<.001$)
Additional injury	1.08 (0.96, 1.21; $p=.21$)	1.19 (1.06, 1.34; $p=.003$)	1.25 (1.11, 1.41; $p=<.001$)
Open fracture	0.91 (0.72, 1.17; $p=.43$)	0.98 (0.77, 1.27; $p=.89$)	1.04 (0.81, 1.35; $p=.78$)
Additional surgery within 7 d	1.04 (0.79, 1.44; $p=.81$)	1.04 (0.79, 1.45; $p=.79$)	1.09 (0.82, 1.53; $p=.57$)
RA	1.24 (1.14, 1.35; $p=<.001$)	1.15 (1.05, 1.26; $p=.001$)	1.16 (1.06, 1.27; $p=.001$)

Appendix Table 3. Adjusted odds of opioid fill and refill. Odds ratio (95% CI) displayed. *p* Values from multivariable modeling.

Factors	Discharge to 2-week opioid refill	Two- to six-week opioid fill	Six-week to ninety-day opioid fill
Age (years)	0.99 (0.98, 1; $p = .002$)	0.99 (0.98, 1; $p = .04$)	0.99 (0.98, 1; $p = .26$)
Female sex	1.27 (0.96, 1.69; $p = .098$)	0.87 (0.65, 1.16; $p = .33$)	1.76 (1.22, 2.54; $p = .002$)
Caucasian race	0.97 (0.74, 1.27; $p = .8$)	1.71 (1.27, 2.32; $p = <.001$)	1.19 (0.84, 1.7; $p = .33$)
BMI (kg/m^2)	1.03 (1.01, 1.04; $p = .007$)	1.02 (1, 1.04; $p = .062$)	1 (0.97, 1.02; $p = .87$)
Smoking	2.19 (1.62, 2.98; $p = <.001$)	3.22 (2.36, 4.38; $p = <.001$)	1.73 (1.16, 2.56; $p = 0.006$)
Pre-operative opioid usage	0.88 (0.57, 1.32; $p = .54$)	3.21 (2.22, 4.62; $p = <.001$)	6.89 (4.67, 10.17; $p = <.001$)
ASA 3 or greater	1.3 (0.99, 1.71; $p = .055$)	0.71 (0.53, 0.94; $p = .018$)	0.56 (0.4, 0.79; $p = .001$)
High energy mechanism	3.3 (2.48, 4.4; $p = <.001$)	1.33 (0.97, 1.81; $p = .074$)	2.47 (1.72, 3.54; $p = <.001$)
Additional injury	0.98 (0.73, 1.3; $p = .87$)	1.9 (1.41, 2.55; $p = <.001$)	3.02 (2.17, 4.2; $p = <.001$)
Open fracture	0.8 (0.42, 1.45; $p = .47$)	1.31 (0.72, 2.32; $p = .36$)	1.74 (0.95, 3.12; $p = .067$)
Additional surgery within 7 d	1.47 (0.75, 3.14; $p = .29$)	1.58 (0.78, 3.44; $p = .23$)	0.72 (0.29, 1.43; $p = .39$)
RA	1.39 (1.1, 1.75; $p = .005$)	0.59 (0.46, 0.74; $p = <.001$)	0.9 (0.68, 1.2; $p = .47$)

Appendix Table 4. Unadjusted inpatient oxycodone 5-mg equivalents consumed in patients with and without RA. Red coloring highlights statistical significance. Median (Q1, Q3) displayed. *p* Values from Wilcoxon rank-sum test.

Outcomes	All subjects ($n = 969$)	Without RA ($n = 105$)	With RA ($n = 864$)	*p* Value
0–24 h post-op	8 (4, 17.4)	14.1 (7.3, 19.9)	5.8 (2.7, 10.1)	<.001
24–48 h post-op	6.7 (3, 15)	13.1 (6, 20)	5 (2, 9.5)	<.001
48–72 h post-op	6.3 (1.3, 11)	9.8 (5.7, 15.1)	2 (0.7, 8)	<.001

Appendix Table 5. Unadjusted outpatient oxycodone 5-mg equivalents prescribed in patients with and without RA. Red coloring highlights statistical significance. Median (Q1, Q3) displayed. *p* Values from Wilcoxon rank-sum test.

Outcomes	All subjects ($n = 969$)	Without RA ($n = 105$)	With RA ($n = 864$)	*p* Value
1 month pre-op to 2 weeks	72 (40, 120)	75 (40, 120)	72 (40, 120)	.76
1 month pre-op to 6 weeks	75.7 (42, 130.7)	90 (50, 170)	74.8 (42, 130)	.135
1 month pre-op to 90 d	80 (43.3, 140)	90 (50, 200)	76.8 (43.3, 135)	.138

Appendix Table 6. Unadjusted rates of outpatient opioid fill and refill. Proportion (percentage) displayed. *p* Value from Fisher's exact test.

Outcomes	All subjects ($n = 969$)	Without RA ($n = 105$)	With RA ($n = 864$)	*p* Value
Discharge to 2-week opioid refill	240/969 (24.8%)	31/105 (29.5%)	209/864 (24.2%)	.23
Two-week to six-week opioid fill	173/969 (17.9%)	34/105 (32.4%)	139/864 (16.1%)	<.001
Six-week to ninety-day opioid fill	131/969 (13.5%)	21/105 (20%)	110/864 (12.7%)	.049