Research Square

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Continuous Intravenous Lidocaine Infusions For Pain Relief in Patients with Uncontrolled Acute Postsurgical Pain Requiring Rescue Analgesia

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Abstract

Background

The potential role of intravenous lidocaine infusions in the treatment of acute postsurgical pain is still incompletely understood. Whether intravenous lidocaine can be used as a rescue intervention in patients experiencing challenging to control postoperative pain has not been properly addressed.

Methods

Observational study using retrospective chart review following approval of the Institutional Review Board. The study cohort were adult patients reporting uncontrolled pain following elective, non-cardiac surgery at a tertiary academic center. Patients were started on continuous intravenous lidocaine infusions on postoperative day 1 or later. We analyzed the longitudinal changes in pain scores (NRS) and opioid use using a linear mixed-effects model.

Results

We analyzed 107 cases. Most patients had a history of chronic pain, chronic opioid use (81%), and reported NRS of 7.8 ± 1.1 before lidocaine initiation. After infusion initiation, 45.4% of patients experienced a NRS decrease of more than 2 points within 12–24 hours. Pain scores did not increase again after lidocaine infusion cessation (6.0 ± 2.1 vs 6.3 ± 2.2). The improvements in pain scores and opioid use in the days after surgery were seen independent of the timing and duration of lidocaine infusions. Potential adverse events (AEs) occurred in 49.5% of infusions and contributed to early discontinuations of lidocaine infusions in 27.1% of the cases.

Conclusions

In patients experiencing initially challenging pain control following major surgery, continuous intravenous lidocaine infusions were associated with improved pain control and decreased opioid use. However, subgroup analyses did not provide strong evidence for a clear analgesic effect directly attributable to lidocaine. While severe AEs were rare, frequent nonspecific AEs led to premature infusion discontinuation further limiting the efficacy and utility of postoperative lidocaine infusions.

Background

Continuous intravenous lidocaine infusions are commonly used in the management of acute postsurgical pain despite a striking lack of evidence that they improve postoperative pain in a substantial manner. Lidocaine is known to have molecular mechanisms that would explain the reported anti-nociceptive and anti-inflammatory effects [1,2], but since a Cochrane analysis published in 2008 reported

that perioperative lidocaine infusions do not achieve a relevant pain reduction at 24 and 48 hours after surgery [3], the practice of using lidocaine infusions in the perioperative setting has become increasingly controversial. However, almost all previously published studies investigated the effects of intraoperative lidocaine infusions on postoperative pain with only a smaller number of these studies extending infusions into the postoperative period. By the time postoperative pain was assessed, the lidocaine infusions had often long been discontinued. These findings could therefore be interpreted as providing evidence for a lack of preventive analgesic properties, but they do not provide strong evidence for lidocaine's lack of direct analgesic effects.

The question whether starting a postoperative continuous lidocaine infusion reduces postoperative pain has received little attention. This is surprising, considering the well described analgesic effects of lidocaine infusions in the treatment of other acute pain states [4]. So far, the evidence for improvements in pain control after lidocaine infusions had been started after surgery is limited to reported subgroups in observational studies [5,6].

In order to provide further evidence for the analgesic effectiveness of postoperative lidocaine infusions in situations of challenging pain control after surgery, we performed a retrospective chart review in patients who received continuous intravenous lidocaine infusions for postoperative pain management in our institution. The chart review focused on patients reporting uncontrolled pain after surgery, not adequately responding to standard pain management, that were subsequently started on a systemic lidocaine infusion.

Methods

Setting

Retrospective observational study using chart review at a single tertiary academic center. We collected patient data from the Electronic Health Record to identify all adult patients who were started on continuous intravenous lidocaine infusions on postoperative day 1 or later and were followed by our institution's inpatient acute pain service following elective, non-cardiac surgery from January 2020 to September 2025.

Ethics Approval and Consent to Participate

The study was approved by the University of California, San Francisco Institutional Review Board (IRB) (IRB# 21-34480). Individual patient consent was waived by the University of California, San Francisco Institutional Review Board. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Data management followed the patient data protection regulations of the Health Insurance Portability and Accountability Act (HIPAA). The study was not registered on clinicaltrials.gov as it is not meeting the definition of an interventional trial. The submitted manuscript adheres to the guidelines outlined in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist.

Patient Selection

Cases were included in our analysis if they met the following criteria: adult patients reporting uncontrolled pain with NRS ≥6 following elective, non-cardiac surgery. Lidocaine infusion started on postoperative day 1 or later, after the medical decision was made that standard pain management did not provide adequate analgesia. Patients needed to be followed by our institution's acute pain service and received infusions on acute care floors.

Exclusion criteria were: indications for lidocaine not related to pain management (such as control of dysrhythmias), use of intravenous lidocaine in procedural areas and operating rooms. To exclude the confounding effects of medical and surgical complications, we excluded patients who were admitted three days or earlier before the surgery date, who came to the operating room from the ICU, who were having additional procedures within five days of the index surgery, and patients who remained in intensive care units for the duration of the lidocaine infusion for medical reasons. Patients were identified through chart review of our Electronic Health Record (APeX, Epic Systems, Madison, WI, USA).

Continuous Intravenous Lidocaine Infusion Protocol

Continuous intravenous lidocaine infusions on acute care floors were clinically introduced in our institution in January 2020. These continuous lidocaine infusions for pain management on acute care floors are exclusively managed by providers of the acute, chronic, or palliative pain service.

Our institutional protocol followed at that time published recommendations and allows lidocaine infusions up to 2 mg/kg/h (adjusted body weight) for maximal 48 hours, without administration of a loading dose. Exclusion criteria for continuous lidocaine infusions include sensitivity or allergy to lidocaine, concurrent use of regional anesthesia, cardiac conduction abnormalities and cardiac failure (defined as ejection fraction < 20%), severe hepatic impairment (defined as bilirubin > 1.46 mg/dl or diagnosis of liver cirrhosis), severe renal impairment (defined as GFR < 30mL/min or ESRD), seizure disorders, and acute porphyria.

The most common indications for continuous lidocaine infusions are uncontrolled pain with routine pain management, pain management of severe pain in patients not tolerating IV ketamine infusions, patients with contraindications for epidural analgesia, patients with unplanned conversion from laparoscopic to open abdominal procedures, patients with severe opioid tolerance or not tolerating opioid therapy, and increasingly, patient and provider preference. Of note, our institution has no Enhanced Recovery After Surgery (ERAS) pathways that include continuous lidocaine infusions. Continuous lidocaine infusions are only ordered 'as needed' when pain management is considered challenging.

Data Collection and Statistics

Data on pain, sedation, and delirium scores were manually extracted from the HER and are presented as mean values in 12-hour intervals. Oral morphine equivalents are reported as daily equivalents, each

representing a calendar day. Only complete days are being reported. Data on adverse events were obtained by screening consult and event notes, as well as review of medication administrations.

Descriptive statistics are being reported as mean ± standard deviation. We analyzed the longitudinal changes in pain scores and opioid use using a **linear mixed-effects model** (Prism, GraphPad Software, Inc, La Jolla, CA). Repeated measurement intervals over time were compared to the pre-infusion time interval.

In order to better define the impact of lidocaine infusions on pain scores and opioid use, several additional comparisons were performed. Average NRS scores in the 12 hours before and after lidocaine infusion discontinuation were compared using paired t-tests to investigate whether rebound pain occurred with infusion stops. In addition, we tried to identify whether the length of lidocaine infusion had an impact on pain scores and opioid use by comparing patients who received lidocaine for less than 24 hours to those who received lidocaine infusions for more than 24 hours. To investigate whether the timing of the infusion start affected the impact of the infusions, we compared the trajectories of opioid use in different subgroups of patients, based on the postoperative day the lidocaine infusion was started.

Differences when compared were considered statistically significant with a significance threshold of $p < 0.05$. Due to the exploratory, hypothesis-generating nature of the study, the data analysis and statistical plan was written after the data were accessed.

Results

Between January 2020 to September 2025, we identified 779 patients that had orders placed for continuous intravenous lidocaine infusions outside of anesthesia care. Of these, 636 cases did not meet the inclusion criteria for this analysis and 36 cases were excluded due to missing data, resulting in 107 cases remaining for analysis (Fig. 1, STROBE analysis).

Patient demographics are summarized in Table 1, revealing a patient population with a high incidence of chronic pain and chronic opioid use. Most patients underwent complex spine or abdominal procedures, resulting in a high number of planned ICU admission following surgery and hospital stays exceeding a week duration.

The average time from surgery end to lidocaine infusion start was 50.7 ± 38.9 hours. Lidocaine infusions were started on various postoperative days as late as on postoperative day 7.Most infusions were started on acute care floors, with a subset of infusions being started in ICUs or, in one case, a TCU, with the patients being subsequently transferred to acute care floors. The average infusion rate at therapy initiation was 1.30 ± 0.35 mg/kg/h (based on adjusted body weight). Infusion characteristics are summarized in detail in table 2.

Patients receiving postoperative lidocaine infusions experienced reductions in opioid use and pain scores following infusion start (table 3). In the 12 to 24 hour period following lidocaine infusion start, 45.5% of patient reported an average improvement of NRS scores by more than 2 points, a clinically important improvement in pain. The improvements in pain scores and reductions in opioid use were not associated with changes in sedation or delirium scores.

When lidocaine infusions were discontinued, pain scores in the 12 hours after infusion stoppage did not increase when compared to the 12 hour interval before infusion stoppage, suggesting absence of rebound pain. Patients who had lidocaine infusions discontinued earlier than initially planned within less than 24 hours saw similar reductions in pain scores and opioid use on the second day after infusion start as those patients who had lidocaine infusions lasting more than 24 hours.

When comparing patients who had their lidocaine infusions started on postoperative day 1, day 2, day 3, or day 4 or later, the trajectories of OME reduction over the postoperative period were similar, with the impact of the lidocaine infusion not being discernable (Figure 2).

Potential adverse events (Aes) are summarized in Table 4. Adverse events were observed in 49.5% of the patients who had received lidocaine infusions. Of these adverse events, 14.0% were rated as mild, 40.2% as moderate, and 0.9% as severe. The most commonly seen Aes were altered mental status (16.8%), sedation (15.0%), and nausea/vomiting (8.4%). The one severe AE identified was a case of loss of consciousness which was not directly attributed to lidocaine toxicity. The rapid response team was called six times in this patient cohort for potential Aes. Patients were transferred to the ICU on three occurrences, and the TCU on one occurrence. Observed adverse events resulted in early infusion discontinuation of lidocaine infusions in 27.1% of cases.

Discussion

This retrospective observational study demonstrates that in a patient population struggling to achieve acceptable pain control after major surgery, starting an intravenous lidocaine infusion was followed by improvements in pain scores and opioid use. These improvements in analgesia were achieved without worsening sedation or delirium scores, and while adverse events were commonly seen in this population, they were mostly non-specific and, in most cases, unlikely to be attributable to the lidocaine infusions.

Similar improvements of analgesia by postoperative lidocaine infusions have been reported before: two observational trials investigating the effectiveness and safety of postoperative lidocaine infusions reported subgroups who had the lidocaine infusions started after surgery end to address uncontrolled pain [5,6]. Both studies reported clinically significant improvements in pain control. However, the lack of a comparison group in the observational trial design does not reliably rule out that the seen improvements are predominately reflective of the improvements routinely seen with recovery from surgery.

Additional comparisons in our study, with the goal to detect signals for the analgesic impact of lidocaine beyond the natural course of recovery, failed to provide further evidence for lidocaine's added analgesic

effects: planned or unplanned discontinuations of lidocaine infusions did not result in worsening pain once the lidocaine infusions were stopped. This lack of rebound pain could indicate that the improvement in pain control the patients displayed are not attributable to the direct analgesic effects of the lidocaine infusions.

When patients were started on lidocaine infusions, the intended infusion protocol was to maintain these infusions for 48 hours. However, a large number of patients had their lidocaine infusions stopped earlier, in most cases due to adverse events that were attributed to the infusions. The comparison of patients who had infusions for less than 24 hours versus those patients who had these infusions for more than 24 hours revealed that both groups had similar pain score and opioid use reductions in the days after lidocaine infusion start. This lack of a more pronounced impact of longer running lidocaine infusions also suggests an only minor analgesic effect on the pain trajectories of the patients.

When comparing the reductions of postoperative opioid use over the course of seven postoperative days, the days when lidocaine infusions were started were not associated with more pronounced improvements in opioid use when compared to the days prior to infusion start. These findings, while not definite proof for lack of effectiveness of postoperative lidocaine infusions, also suggest that the impact of these infusions may be limited.

The lack of a comparison group not receiving lidocaine infusions complicates the interpretation of lidocaine analgesic effects. The intensity of pain reported in our cohort precluded a placebo comparison for ethical reasons. There is a striking lack of published information on the expected pain trajectories in patients with severe postoperative pain. One published study reported a median time of 96 hours to achieve acceptable pain scores with movement in patients with chronic pain [7]. But most of the patients in that study received continuous regional anesthesia and reported lower postoperative pain scores, so longer recovery times had to be anticipated in our study cohort. It remains unclear whether the use of lidocaine infusions accelerated recovery.

The question whether lidocaine infusions improve postoperative pain is of critical importance. Considering the ongoing debate over the safety of continuous lidocaine infusions, the effectiveness of these interventions needs to be proven without doubt to justify their application. While the use of lidocaine infusions has generally been considered safe [8] and a potentially safer alternative to opioid use [9], there have been fatalities reported in patients receiving lidocaine that have been clearly [10] or potentially [11] related to the administration of toxic doses of lidocaine. As a consequence, amid an ongoing controversy, the use of IV lidocaine has also repeatedly been labeled unsafe and to be avoided [12,13]. And in addition to the potential risk of rare but serious adverse events, intravenous lidocaine infusions have commonly been held responsible for less serious adverse events in the postoperative period.

In our cohort, potential adverse events were reported in half of patients, resulting in over a quarter of infusions being discontinued prematurely. The commonly reported AEs, including altered mental status,

sedation, and nausea, are frequently reported events in the postoperative period and are difficult to attribute to lidocaine toxicity. When used as a rescue analgesic in a complex postsurgical population, lidocaine is often introduced concomitantly with opioids, gabapentinoids, ketamine, and other agents similar side effect profiles, as seen in our analysis. Nonetheless, the frequent occurrence of adverse events that may not even be causally linked to the lidocaine infusion, but where a contributing role of lidocaine cannot clearly be ruled out, in combination with safety concerns of involved providers often results in early therapy discontinuations. This further limits the acceptability and subsequently the effectiveness of these infusions.

However, the whole controversy about the safety of lidocaine infusions becomes rather pointless if no strong evidence can be provided for the analgesic effectiveness of lidocaine infusions. The impact of intraoperative lidocaine infusions on postoperative pain has been repeatedly questioned, and when beneficial effects were reported they seemed to be of short duration [3,14]. This could be the result of lidocaine not achieving prolonged analgesia by blocking the mechanisms of central sensitization [15]. But a lack of such preventive analgesic effects does not exclude the possibility that lidocaine's direct analgesic effects could be of benefit when postoperative infusions are being used for an extended period. The evidence supporting this claim comes predominately from observational studies and remains rather speculative. However, extending intraoperatively started lidocaine infusions into the postoperative period for 24 hours or longer did not result in better pain-related outcomes beyond the early postoperative period [3], strongly suggesting also a lack of direct analgesic benefit of these infusions.

Our study, similar to earlier studies, is limited by its retrospective, observational design. We attempted to overcome this limitation by trying to identify differences in subgroups of our cohort. And while the overall cohort demonstrated improvements in pain that could be interpreted as attributable to the intervention, our observations in these subgroup analyses questions this conclusion. The fact that stopping the infusions or the length of the lidocaine infusions seem to have little impact on pain scores and opioid use suggest little impact of the infusions itself. Similarly, when looking at subgroups with different start times of lidocaine infusions, the trajectories of opioid use were similar between subgroups. This observation suggests that the lidocaine did not significantly enhance the recovery from postoperative pain when started.

Our subgroup analyses are limited by their group size and underpowered to assess subtle differences. The subgroup with shorter lidocaine infusion durations may include some patients that may already have been improving independent of the infusions, resulting in the early discontinuation not being triggered by side effects. And rebound pain may not be occurring with the discontinuation of a preventive analgesic, but as discussed earlier, the preventive analgesic effects of lidocaine are questionable. Lastly, the chosen patient population with a large number of opioid tolerant, chronic pain patients, now experiencing acute on chronic pain, is not very likely to experience dramatic improvements with any type of intervention. However, these patients are the real-world scenario where intravenous lidocaine infusions are most commonly used.

In summary, our observational trial, despite noticeable improvements in pain scores and opioid use following the start of lidocaine infusions, fails to provide strong evidence that intravenous lidocaine significantly accelerates achieving improvements in analgesia. Considering the ongoing controversy about the safety of these infusions, their use remains questionable until well designed comparative studies demonstrate their analgesic impact in postoperative pain management. Due to a potential lack of major analgesic impact, placebo-controlled, randomized trials seem ethically justifiable.

Declarations

Ethics approval and consent to participate

Individual patient consent was waived by the UCSF Institutional Review Board.

IRB # 21-34480

Consent for publication

Not applicable

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions:

MB: Conceptualization, Data Curation, Formal Analysis, Methodology, Supervision, Writing – Original Draft

JK: Data Curation, Formal Analysis, Investigation, Writing – Review and Editing

SM: Conceptualization, Methodology, Resources, Writing – Review and Editing

CA: Conceptualization, Methodology, Resources, Writing – Review and Editing

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Tables

Table 1: Patient Characteristics

Patient Characteristics	
n	107
Sex, Female, n (%)	71 (66.4)
Age, mean (SD)	56.71 (12.68)
Weight [kg], mean (SD)	82.97 (23.37)
BMI, mean (SD)	28.58 (7.21)
ASA Status	
I, n (%)	1 (0.9)
II, n (%)	49 (45.4)
III, n (%)	57 (52.8)
IV, n (%)	0 (0.0)
Home Opioid Use, n (%)	87 (80.6)
Preoperative NRS score, mean (SD)	5.12 (3.27)
ICU Admission Postoperatively, n (%)	33 (30.6)
Length of Stay Postoperatively, days (SD)	10.32 (7.16)
Surgery Type, n (%)	
Spine	60 (55.6)
General Surgery	25 (23.1)
Surgical Oncology	10 (9.3)
Orthopedics Non-Spine	3 (2.8)
Neurosurgery Non-Spine	1 (0.9)
Others	8 (7.4)

Table 2: Infusions Characteristics

Infusion Characteristics	
Infusion Initiation Location, n (%)	
Acute Care Floor	89 (82.4)
ICU	14 (13.0)
TCU	4 (3.7)
Mean Time from Surgery to Infusion Start, h (SD)	50.66 (38.89)
Day of Infusion Start, n (%)	
Postoperative Day 1	49 (45.4)
Postoperative Day 2	25 (23.1)
Postoperative Day 3	15 (13.9)
Postoperative Day 4+	18 (16.7)
Mean Infusion Duration, h (SD)	35.01 (16.58)
0-8h, n (%)	10 (9.3)
8-24h, n (%)	22 (20.4)
24-48h, n (%)	52 (48.1)
48+h, n (%)	24 (22.2)
Mean Infusion Rate at Initiation, mg/kg/h (SD)	
Actual Body Weight	1.11 (0.33)
Adjusted Body Weight	1.30 (0.33)
Ideal Body Weight	1.45 (0.39)
Concomitant Analgesics, n (%)	
Acetaminophen	104 (96.3)
Opioids	104 (96.3)
Gabapentinoids	75 (69.4)
Ketamine	54 (50.0)
Muscle Relaxants	66 (61.1)
NSAIDs	18 (16.7)
Antidepressants	30 (27.8)

Table 3:Treatment Outcomes

Treatment Outcomes		
Pain Score (NRS)	**mean (SD)**	**p**
-12 to 0h (pre-infusion)	7.82 (1.12)	
0 to 12h	6.53 (1.81)*	<0.001
12 to 24h	5.89 (2.09)*	<0.001
24 to 36h	6.10 (2.00)*	<0.001
36 to 48h	6.03 (2.32)*	<0.001
48 to 60h	6.27 (1.94)*	<0.001
Patients with Clinically Important NRS Improvement (decrease of mean NRS by 2 score points or more)	**n (%)**	
0 to 12h	32 (29.9)	
12 to 24h	44 (45.4)	
24 to 36h	31 (38.3)	
36 to 48h	28 (37.8)	
48 to 60h	30 (30.3)	
POSS	**mean (SD)**	
-12 to 0h (pre-infusion)	0.85 (0.34)	
0 to 12h	0.85 (0.35)	
12 to 24h	0.82 (0.33)	
24 to 36h	0.84 (0.30)	
36 to 48h	0.79 (0.29)	
48 to 60h	0.82 (0.23)	
NuDesc	**mean (SD)**	
-12 to 0h (pre-infusion)	0.11 (0.38)	
0 to 12h	0.27 (0.80)	
12 to 24h	0.24 (0.61)	
24 to 36h	0.34 (0.89)	
36 to 48h	0.38 (0.84)	
48 to 60h	0.21 (0.67)	

OME	mean (SD)	p
Day of Infusion Start	412 (411)	
1 Day after Infusion Start	349 (401)*	0.013
2 Days after Infusion Start	276 (288)*	<0.001
3 Days after Infusion Start	254 (266)*	<0.001
4 Days after Infusion Start	266 (308)*	<0.001

Table 4: Complications

Complications	n (%)
Any Potential Adverse Event	54 (50.5)
Mild	15 (14.0)
Blurred Vision	3 (2.8)
Drowsiness	2 (1.9)
Perioral Numbness	2 (1.9)
Metallic Taste	2 (1.9)
Tinnitus	2 (1.9)
Dyesthesia/Paresthesia	2 (1.9)
Weakness	2 (1.9)
Spaced Out	1 (0.9)
Dizziness	1 (0.9)
Headache	1 (0.9)
Moderate	43 (40.2)
Altered Mental Status	18 (16.8)
Somnolence/Sedation	16 (15.0)
Nausea/Vomiting	9 (8.4)
Diplopia	2 (1.9)
Hypotension	2 (1.9)
Sinus Bradycardia	2 (1.9)
Word-finding Difficulty	1 (0.9)
Hearing Change	1 (0.9)
Tremor	1 (0.9)
Hypertension	1 (0.9)
Severe	1 (0.9)
Loss of Consciousness	1 (0.9)
Early Discontinuation due to Adverse Event	29 (27.1)
Rapid Response Called	6 (5.6)
Escalation of Care	4 (3.7)

Transfer to ICU	3 (2.8)
Transfer to TCU	1 (0.9)

Figures

Figure 1

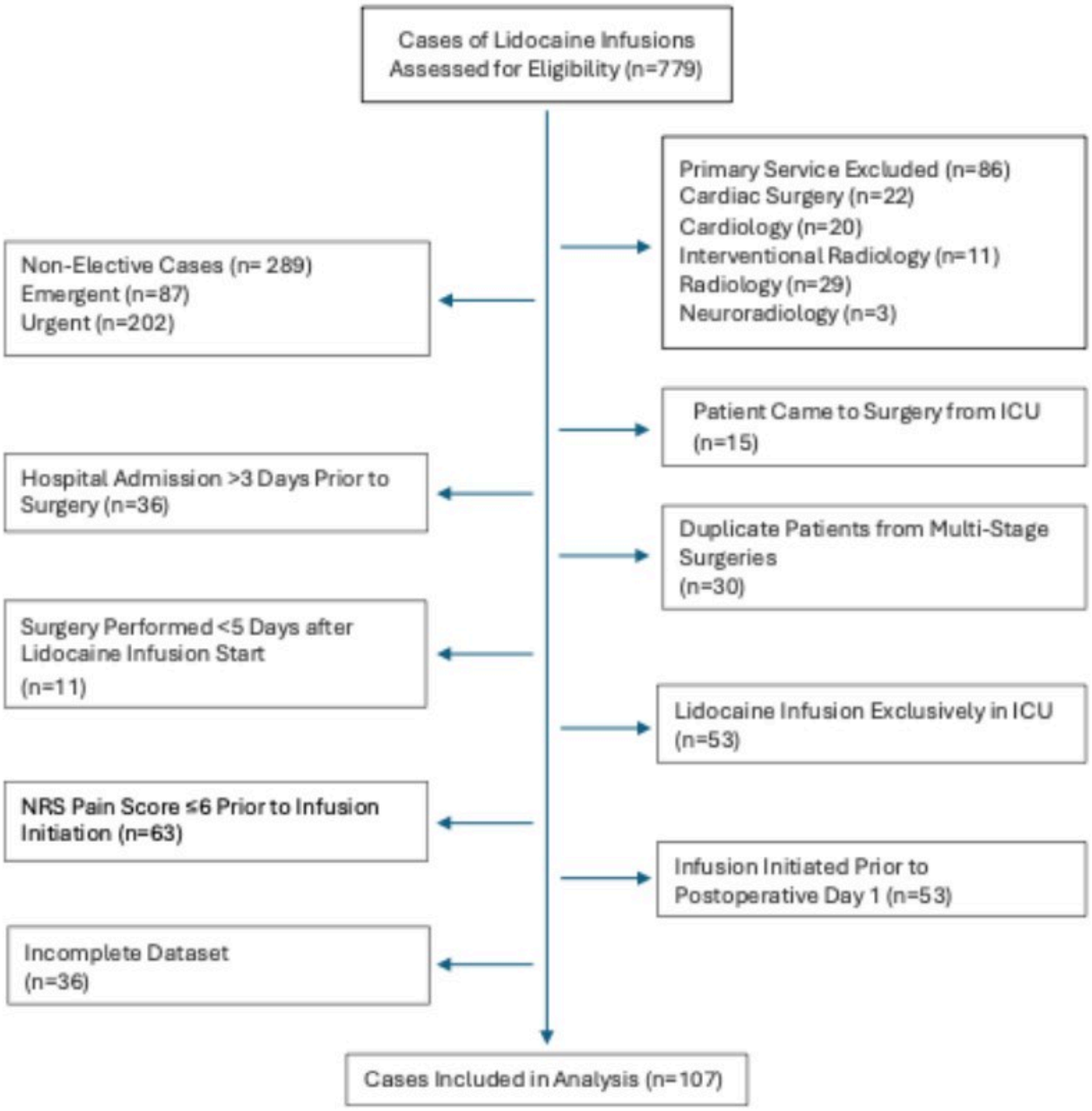

Figure 1

STROBE Chart

Figure 2

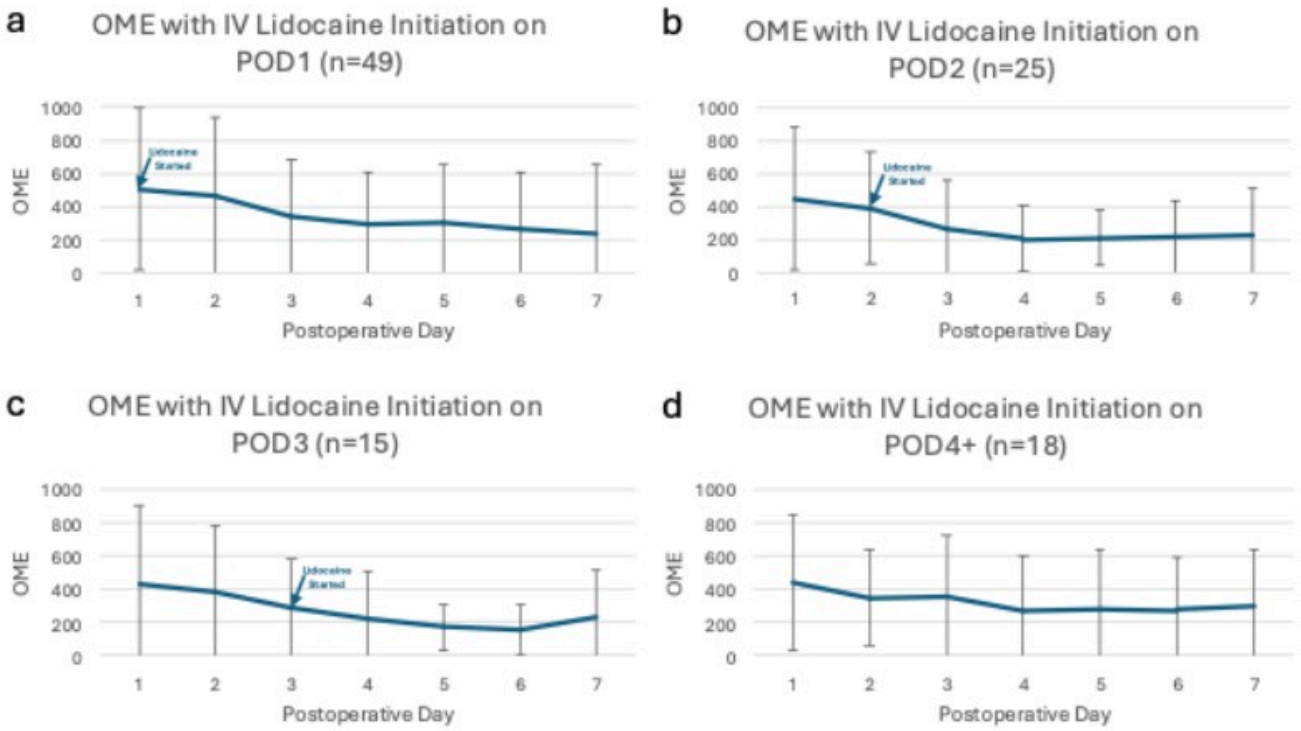

Figure 2

Documented oral morphine equivalents (OME) reported on postoperative days 1 to 7. Patients being started on lidocaine infusions on postoperative day 1 (a), 2 (b), 3 (c) or later (d) showed similar OME trajectories.