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Original Research Article

Pain Intensity in the First 96 Hours After Abdominal Surgery: A Prospective Cohort Study

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Abstract

Objective. Multimodal pain management strategies aim to improve postoperative pain control. The purpose of this study was to analyze pain scores and risk factors for acute postoperative pain after various abdominal surgery procedures. **Methods**. Data on 11 different abdominal surgery procedures were prospectively recorded. Pain intensity (rest, mobilization) and patient satisfaction at discharge were assessed using a visual analog scale (VAS; 0–10), and analgesic consumption was recorded until 96 hours postoperation. Demographic, surgery-related, and pain management–related univariate risk factors for insufficient pain control (VAS $\geq$ 4) were entered in a multivariate logistic regression model. **Results**. A total of 1,278 patients were included. Overall, mean VAS scores were <3 at all time points, and scores at mobilization were consistently higher than at rest ($P < 0.05$). Thirty percent of patients presented a prolonged VAS score $\geq$4 at mobilization at 24 hours, significantly higher than at rest (14%, $P < 0.05$). High pain scores correlated with high opioid consumption, whereas a variability of pain scores was observed in patients with low opioid consumption. The only independent risk factor for moderate and severe pain (VAS $\geq$ 4) was younger age (<70 years, $P = 0.001$). The mean satisfaction score was 8.18 $\pm$ 1.29. **Conclusions**. Among 1,278 patients, pain was controlled adequately during the first four postoperative days, resulting in high levels of patient satisfaction. Pain levels were higher at mobilization. Younger age was the only independent risk factor for insufficient pain control. Preventive treatment in patients <70 years old and before mobilization could be evaluated for potential improvement.

Key Words: Postoperative Pain; Abdominal Surgery; Multimodal Therapy

Introduction

Pain management is essential in improving recovery and reducing postoperative hospital stay [1]. Multimodal pain management has been endorsed by enhanced recovery after surgery (ERAS) protocols, aiming to decrease postoperative morbidity by decreasing surgical stress and maintaining functional capacity [2–5]. Opioid-sparing multimodal pain therapy has become a key component of ERAS care [6] and is now routinely practiced for a variety of diverse surgeries in the perioperative period [7,8]. ERAS includes the concomitant application of regional and systemic analgesia with the aim of decreasing postoperative pain scores and opioid consumption [9]. For surgeries performed outside ERAS protocols, standardized care maps endorse principles of multimodal pain management [10]. Interestingly, actual pain scores and consumed analgesics have rarely been assessed and reported beyond 24 hours after surgery within a large cohort of patients.

The aims of the present study were 1) to assess analgesic consumption and pain scores at rest and at mobilization and 2) to identify risk factors for acute postoperative pain peaks in the first 96 hours after various abdominal surgeries in an ERAS center with diverse surgical activity.

Methods

Study Design

The prospective pain database was considered a quality improvement project, and informed consent was waived by the institutional review board, Swiss ethics committee CER-VD (Commission Cantonale d'Éthique de la Recherche sur l'Être Humain). Written confirmation of this decision was provided by July 10, 2015. A general consent for research was collected for every patient before his or her operation (Supplementary Data). The study was performed and analyzed in line with the STROBE statement. The quality improvement project was already launched by the time we retrospectively registered the trial under www.researchregistry.com (UIN research registry1556). The authors confirm that all the studies related to this trial are registered.

This is a prospective cohort study including all consecutive adult patients (≥18 years) who underwent 11 predefined elective or emergent surgical procedures in the Department for Visceral Surgery at the University Hospital of Lausanne (CHUV), Switzerland. Patient recruitment and follow-up occurred between January 2014 and April 2015. Exclusion criteria included perioperative mental confusion, communication difficulties due to language restrictions (non-French-speaking), and patients undergoing other surgical procedures. For patients who underwent more than one surgery during the study period, only the first procedure was assessed.

Surgical Procedures

Surgical procedures were grouped by organ systems or surgical sites: colorectal, bariatric, upper gastrointestinal (GI), liver, pancreas, hernia, cholecystectomy, abdominal wall, lymph node dissection (LND), and appendectomy. Thyroid and parathyroid, although apart from the abdominal cavity, were performed by surgeons from the Visceral Department and were therefore also studied. The colorectal group included major open and minimally invasive surgeries like sigmoidectomy, right and left hemicolectomy, total colectomy, rectal resection, and stoma procedures (i.e., ileostomy closure and Hartmann reversal). Bariatric, gall bladder, and appendix surgeries were performed exclusively using a minimally invasive technique. Upper GI procedures consisted of partial or total gastrectomy, reflux surgery, and esophagectomy. In the hernia group, inguinal and umbilical hernia repairs were subgrouped, with or without mesh repair. Abdominal wall procedures comprised mainly postoperative midline hernia mesh repair.

Upper gastrointestinal, liver, pancreas, hernia, (para)-thyroid, and abdominal wall procedures were either performed open or were minimally invasive. Lymph node dissection was only performed open.

Major GI surgery was defined as any esophageal, gastric, hepatic, pancreatic, intestinal, or colorectal resection for benign or malignant disease that was either open or laparoscopic and lasted more than two hours [11].

Bariatric, hernia, cholecystectomy, (para)thyroid, lymph node dissection, and appendectomy were considered minor surgeries.

Analgesics

Intraoperatively, fentanyl, and sufentanyl were administered at the discretion of the anesthesiologist. Every patient received paracetamol 1 g at the end of the procedure unless contraindicated. Perioperative pain treatments could include intravenous (iv) clonidine (0.5–1 ug/kg), iv ketamine (0.25 mg/kg bolus followed by 0.25 mg/kg/h, maximum 1 mg/kg) [12] associated with iv lidocaine (1.5 mg/kg for induction, then 2 mg/kg/h until leaving the recovery room) [13] for major surgeries under laparoscopy or under laparotomy when thoracic epidurals were contraindicated, thoracic epidural analgesia (bupivacaine 0.0625% + fentanyl 2 ug/mL + adrenaline 2 ug/mL) for major open procedures unless contraindicated, spinal anesthesia (bupivacaine 0.5% + fentanyl), transverse abdominal plane (TAP) blocks, and surgical wound infiltration using bupivacaine 0.25% or naropin 0.25%. The numbers of procedures that used iv ketamine, iv lidocaine, thoracic epidural analgesia, and wound infiltration are summarized in Table 1. Colorectal, upper gastrointestinal, liver, pancreas, and bariatric procedures followed the preoperative and postoperative ERAS Society recommendations [14–19]. Specifically for bariatric surgery, patients received fentanyl or sufentanyl intraoperatively, up to a maximum level of 10 ug/kg or 1 ug/kg (according to lean body weight), respectively, followed if needed by a continuous infusion of remifentanil (up to 0.2 ug/kg/min) until the end of surgery. Moreover, iv magnesium sulfate 40 mg/kg (ideal body weight) and iv lidocaine (1.5 mg/kg for induction, then 2 mg/kg/h until leaving the recovery room) were also administered intraoperatively. In the bariatric group, postoperative pain medication consisted of only paracetamol, mefenacid, and tramadol.

Paracetamol, novaminsulfon, nonsteroidal anti-inflammatory drugs (NSAIDs; ibuprofen, mefenacid, ketorolac), and opioids (morphine, oxycodone, buprenorphine, tramadol) were administered postoperatively according to standardized care maps built in our institution for each group of surgeries and based on ERAS guidelines or dosages recognized as efficient in the literature [10, 20]. All medications administered in the recovery room were recorded until 96 hours postoperation.

Oral morphine equivalents were calculated by use of standardized conversion tables [21]: iv (recovery room) or sc (from room arrival, 96 hours) morphine (3x), oral oxycodone (2x), oral buprenorphine (75x), oral tramadol (0.1x). Morphine equivalents were recorded for the following time periods: 24 hours (including in the recovery room until the end of postoperative day [POD] 0), 48 hours, 72 hours, and 96 hours postoperation.

Data Collection

Data were collected prospectively by the surgical and anesthesia team for the intraoperative phase and by a

Table 1. Univariate analysis

Factor, No.	Max VAS < 4 (N = 493), No. (%)	Max VAS ≥ 4 (N = 785), No. (%)	OR (for VAS ≥ 4) (95% CI)	*P* Value
BMI				
<30 kg/m^2 (939)	355 (37.8)	584 (62.2)	1 (ref)	-
≥30 kg/m^2 (339)	138 (40.7)	201 (59.3)	0.885 (0.687 to 1.141)	0.347
Gender				
Female (650)	237 (36.5)	413 (63.5)	1 (ref)	–
Male (628)	256 (40.8)	372 (59.2)	0.834 (0.666 to 1.045)	0.114
Age				
<70 y (960)	349 (36.3)	611 (63.7)	1 (ref)	-
≥70 y (318)	144 (45.3)	174 (54.7)	0.690 (0.534 to 0.892)	0.005
ASA				
I–II (981)	392 (40.0)	589 (60.0)	1 (ref)	–
III–IV (297)	101 (34.0)	196 (66.0)	1.292 (0.984 to 1.695)	0.065
Surgery type				
Colorectal (332)	93 (28.0)	239 (72.0)	1 (ref)	-
Bariatric (73)	13 (17.8)	60 (82.2)	1.795 (0.942 to 3.425)	0.076
Upper GI (58)	16 (27.6)	42 (72.4)	1.021 (0.548 to 1.906)	0.947
Liver (77)	21 (27.3)	56 (72.7)	1.038 (0.595 to 1.809)	0.896
Pancreas (71)	14 (19.7)	57 (80.3)	1.584 (0.842 to 2.980)	0.153
Hernia (57)	34 (59.7)	23 (40.4)	0.263 (0.147 to 0.471)	<0.001
Cholecystectomy (210)	98 (46.7)	112 (53.3)	0.445 (0.310 to 0.639)	<0.001
Abdominal wall (86)	29 (33.7)	57 (66.3)	0.765 (0.461 to 1.270)	0.3
(Para)thyroid (88)	57 (64.8)	31 (35.2)	0.212 (0.129 to 0.348)	<0.001
Lymph node dissection (66)	51 (77.3)	15 (22.7)	0.114 (0.061 to 0.214)	<0.001
Appendectomy (160)	67 (41.9)	93 (58.1)	0.540 (0.364 to 0.802)	0.002
Surgery duration				
<180 min (897)	396 (44.2)	501 (55.9)	1 (ref)	–
>180 min (381)	97 (25.5)	284 (74.5)	2.314 (1.775 to 3.018)	<0.001
Anesthesia duration				
<220 min (894)	397 (44.4)	497 (55.6)	1 (ref)	-
>220 min (384)	96 (25.0)	288 (75.0)	2.396 (1.837 to 3.127)	<0.001
Surgical approach (intention-to-treat)				
Open (584)	240 (41.1)	344 (58.9)	1 (ref)	–
Min. invas./converted (694)	253 (36.5)	441 (63.5)	1.216 (0.970 to 1.524)	0.09
Surgery setting				
Elective (941)	359 (38.2)	582 (61.9)	1 (ref)	-
Emergency (337)	134 (39.8)	203 (60.2)	0.934 (0.724 to 1.206)	0.602
Epidural anesthesia				
No (1,034)	432 (41.8)	602 (58.2)	1 (ref)	–
Yes (244)	61 (25.0)	183 (75.0)	2.153 (1.571 to 2.950)	<0.001
Lidocaine				
No (1,070)	433 (40.5)	637 (59.5)	1 (ref)	
Yes (208)	60 (28.9)	148 (71.2)	1.677 (1.213 to 2.318)	0.002
Ketamine				
No (1,200)	471 (39.3)	729 (60.8)	1 (ref)	–
Yes (78)	22 (28.2)	56 (71.8)	1.645 (0.991 to 2.729)	0.054
Wound infiltration				
No (1,099)	417 (37.9)	682 (62.1)	1 (ref)	
Yes (179)	76 (42.5)	103 (57.5)	0.829 (0.601 to 1.142)	0.25

Presentation of univariate risk factors: patient related (BMI, gender, age, ASA), surgery related (surgery type, surgery duration, anesthesia duration, surgical approach, surgery setting), and related to intraoperative pain management (epidural anesthesia, lidocaine, ketamine, wound infiltration) by comparing patients expressing mild pain (VAS < 4) with patients expressing moderate and severe pain (VAS ≥ 4). *P* values are from a univariate logistic regression model.

ASA = American Society of Anesthesiologists; BMI = body mass index; CI = confidence interval; GI = gastrointestinal; LND = lymph node dissection; OR = odds ratio; VAS = visual analog scale.

dedicated study nurse for the postoperative period. Data entry in the computerized coded database was performed by two members of the anesthesiology care team (MC, CB). Recorded parameters included baseline demographics (age, gender, body mass index [BMI] and American Society of Anesthesiologists score [ASA]), surgical details (open vs laparoscopy, surgery duration, elective vs emergent), and anesthetic details (anesthesia

duration, premedication [midazolam], type [intravenous, volatiles], analgesics, postoperative nausea and vomiting [PONV] medication [dexamethasone, droperidol, ondansetron]). Visual analog scale scores (VAS) were used to measure pain (0 = no pain to 10 = maximal pain) at rest and at mobilization from the recovery room discharge until 96 hours postoperation at different time points: recovery room, upon arrival in ward, two hours, six hours, 12 hours, 24 hours, 36 hours, 48 hours, 72 hours, and 96 hours. A VAS $\geq$4 was defined as moderate to severe pain, as compared with mild pain (VAS $<$ 4) [22]. Overall patient satisfaction with pain management was evaluated at discharge on a scale from 0 (not satisfied at all) to 10 (completely satisfied). Length of stay was recorded from the day of surgery until discharge.

Data were analyzed (univariate and multivariate analysis) as patient related (BMI, gender, age, ASA), surgery related (surgery type, surgery duration, anesthesia duration, surgical approach, elective vs emergency setting), and related to intraoperative pain management (epidural anesthesia, lidocaine, ketamine, wound infiltration) by comparing patients expressing mild pain (VAS $<$ 4) with patients expressing moderate or severe pain (VAS $\geq$ 4) at any time point between the recovery room discharge to 96 hours regardless of rest or mobilization. Among the various surgeries, the reference was colorectal surgery because it comprised the highest number of patients and the largest experience of ERAS care and standardization within our institution [23].

Statistical Analysis

Data analysis was performed using Stata (version 14.1; StataCorp, College Station, TX, USA). Continuous data distribution was analyzed using QQ plots.

Continuous data with Gaussian distribution were summarized as mean ± SD, whereas data with non-Gaussian distribution were summarized as median and interquartile range (IQR). Differences in means for Gaussian-distributed data between the two groups were assessed using the Student *t* test for independent groups, or the Student paired *t* test for paired data. Differences in means for Gaussian-distributed data between more than two independent groups were assessed using ANOVA. Differences in distributions for non-Gaussian data between two independent groups were assessed using the Mann-Whitney-Wilcoxon rank sum test. For paired data with non-Gaussian distribution, Wilcoxon's signed rank test was used. Differences in medians for non-Gaussian data between more than two independent groups were assessed using the Kruskall-Wallis test.

Categorical data were summarized as raw frequencies and relative percentages. Differences in distribution for categorical data between two or more independent groups were assessed using the chi-square test, or the Fisher exact test in case of insufficient sample size. McNemar's test was used to assess the difference in distribution for categorical data between two paired groups.

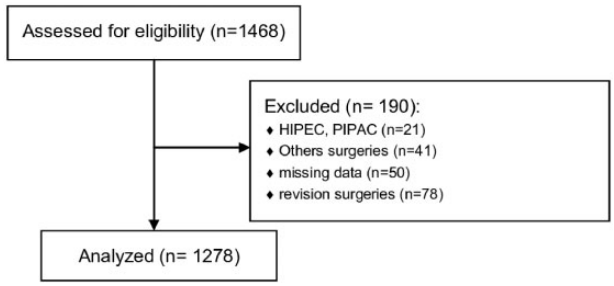

Figure 1. Flow diagram of the study.

Logistic regression modeling was used to evaluate the association between one or more cofactors and a binary outcome. Univariate factors presenting with *P* values $<$0.200 were included in the multivariate analysis.

A *P* value $<$0.05 was considered statistically significant. No statistical correction has been applied to *P* values.

Results

A total of 1,468 consecutive procedures were performed from January 2014 until April 2015 (Figure 1). One hundred ninety operations were excluded from analysis: surgeries with concomitant application of intraoperative chemotherapy like heated intraperitoneal chemotherapy (HIPEC; N = 6) and pressurized intraperitoneal aerosol chemotherapy (PIPAC; N = 15) were not analyzed because of their effects on pain due to chemically induced peritonitis. A few adrenalectomy (N = 11) and proctologic procedures (N = 30) were performed and were hard to group with other surgeries. Consequently, they were not analyzed. The files with missing pertinent data (N = 50) and revision surgeries (N = 78) were also excluded.

The demographic data of the 1,278 eligible and analyzed patients are displayed in Table 1. Overall, mean VAS scores were $<$3 from the recovery room until 96 hours, and statistical differences were found between rest and mobilization at all time points (Figure 2). Similar findings were observed for the different surgeries (Figure 3), with a maximum mean VAS score of 3.31 ± 2.31 for bariatric surgery at mobilization at 24 hours.

The percentages of patients reporting a VAS score $\geq$4 at rest and at mobilization (14% and 30%, respectively) at 24 hours were significantly different ($P < 0.05$, McNemar's test) and remained stable during the observed time span (Figure 4a). The magnitude of difference between a VAS score $\geq$4 at rest and at mobilization over the 96 hours (median value) was 1 (50% of the patients: quantile 75% = 2, quantile 95% = 4) (data not shown). Among the different surgeries, similar findings were observed with maximal VAS score for bariatric surgery patients during mobilization at the 24-hour time point (55%) (Figure 4b). Seven hundred eighty-five patients

presented a maximum VAS score ≥4 during their hospitalization, whereas 493 presented a maximum VAS score <4 (Table1). For those with a maximum VAS score ≥4, 783 experienced it during mobilization whereas two experienced it at rest (data not shown).

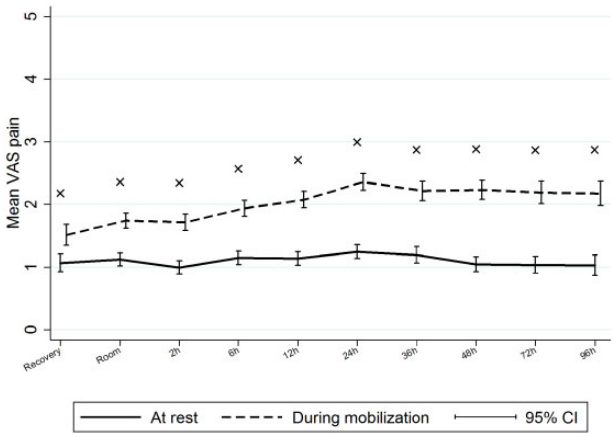

Figure 2. Overall mean visual analog scale (VAS) pain score at rest and mobilization. Illustration of mean VAS pain scores at various time points at rest (continuous line) and during mobilization (dashed line) according to all surgery types. Whiskers indicate the 95% confidence interval, and × represents a statistically significant difference between rest and mobilization ($P < 0.05$, Wilcoxon's signed rank test). CI = confidence interval.

Comparing the maximal VAS pain score for every patient and the total amount of morphine equivalent consumed throughout the hospital stay, high pain scores correlated with a high amount of morphine equivalent consumption (Figure 5a). On the other hand, patients who consumed a low morphine equivalent dosage reported a variability of pain scores. Similar observations regarding high pain scores were made across the different surgeries, specifically in upper GI, liver, and pancreas surgeries (Figure 5b). Similarly, in patients with low morphine equivalent consumption, a high variability of pain scores was reported mainly in bariatric, hernia, and (para)thyroid surgeries.

Univariate risk factors for moderate and severe pain (VAS ≥ 4) were longer duration of surgery and anesthesia (odds ratio [OR] = 2.314, $P < 0.001$, and OR = 2.396, $P < 0.001$, respectively), the presence of epidural analgesia (OR = 2.153, $P < 0.001$), and intravenous lidocaine (OR = 1.677, $P = 0.002$) (Table 1). Older age (≥70) was associated with lower odds of moderate and severe pain (OR = 0.690, $P = 0.005$). Despite some significant results for higher VAS pain scores in women at mobilization at six hours ($P = 0.043$), 24 hours ($P = 0.026$), and 48 hours ($P = 0.019$) (data not shown), overall, no significant difference was observed involving gender as a potential risk factor. Compared with colorectal surgery, patients undergoing five minor surgeries were significantly less likely to report pain scores ≥4; these

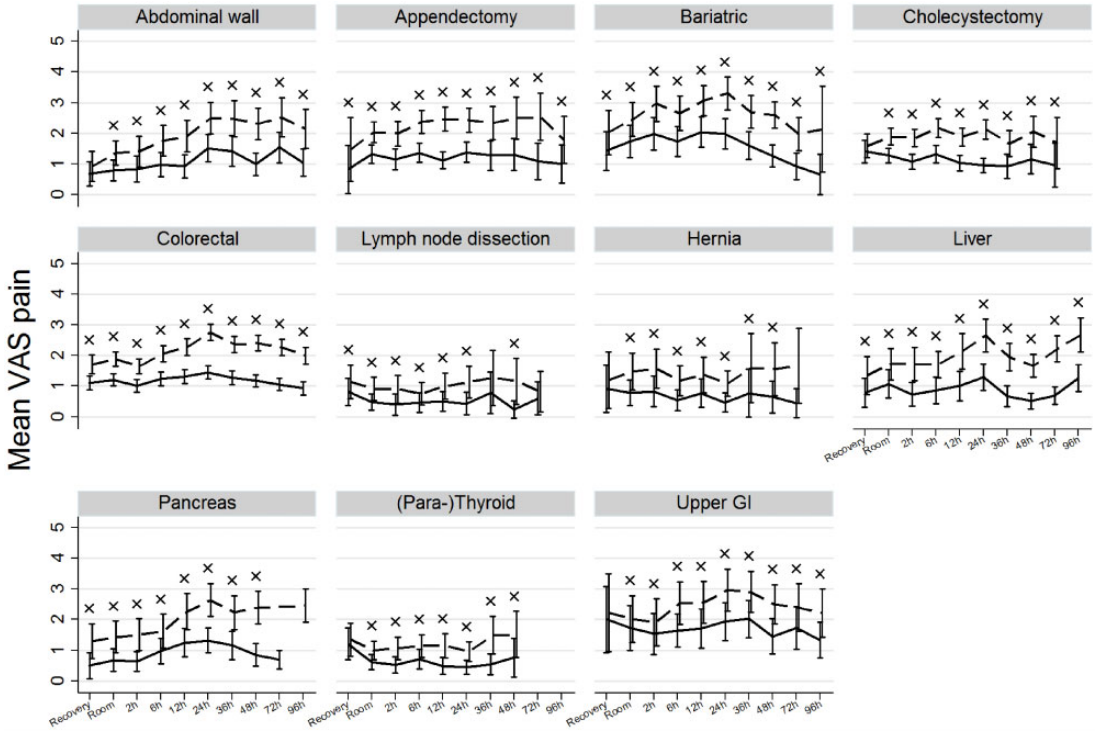

Figure 3. Overall mean visual analog scale (VAS) pain score at rest and mobilization in each type of surgery. Illustration of mean VAS pain scores at different time points at rest (continuous line) and during mobilization (dashed line) according to each type of surgery. Whiskers indicate the 95% confidence interval, and × represents a statistically significant difference between rest and mobilization ($P < 0.05$, Wilcoxon's signed rank test). CI = confidence interval.

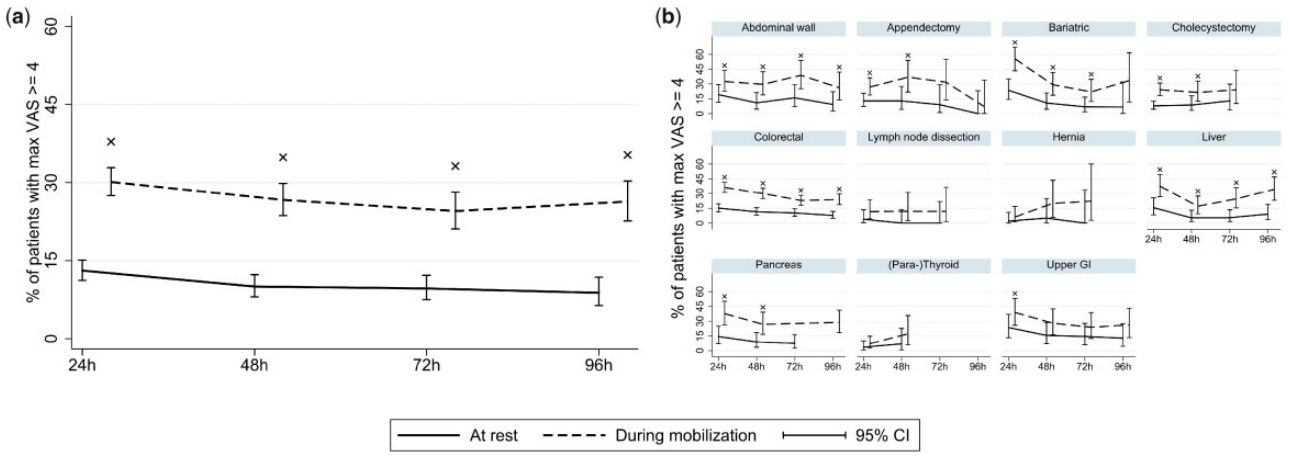

Figure 4. Percentage of mean visual analog scale (VAS) pain score ≥4. Illustration of percentage of patients presenting a VAS pain score ≥4 at 24 hours, 48 hours, 72 hours, and 96 hours at rest (continuous line) and during mobilization (dashed line) according to all surgery types (a) or each type of surgery (b). Whiskers indicate the 95% confidence interval, and × represents a statistically significant difference between rest and mobilization ($P < 0.05$, McNemar's test). CI = confidence interval.

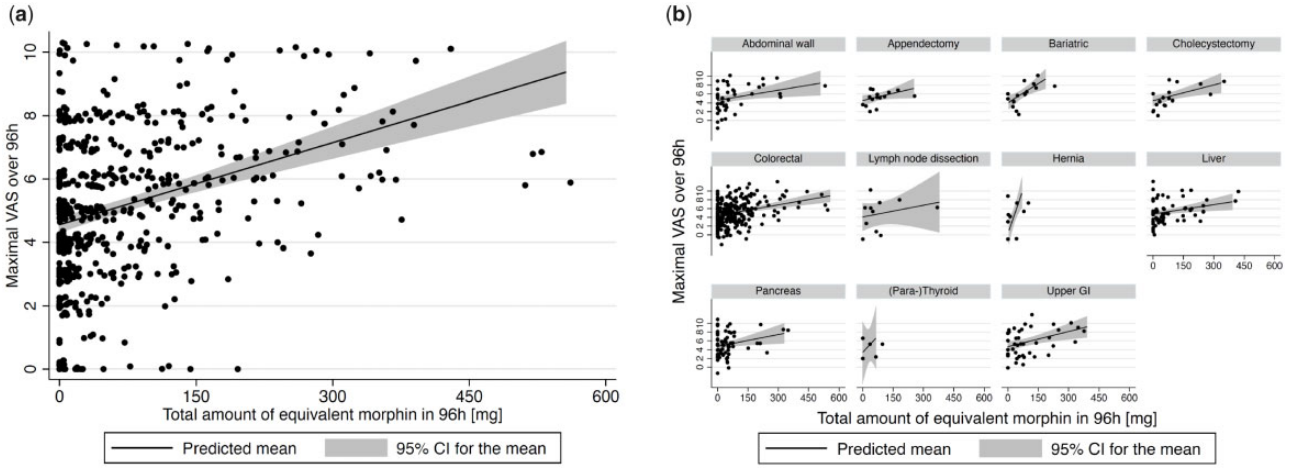

Figure 5. Relation between the maximal visual analog scale (VAS) pain score and the total amount of equivalent morphine consumption. Scatterplot illustration of the maximal VAS pain score over 96 hours for each patient with the total morphine-equivalent dosage (mg) consumed over 96 hours. Descriptions are provided for all types of surgery (a) and for each type of surgery (b). The continuous line illustrates the predicted mean, and the gray indicates the 95% confidence interval for the mean.

included hernia (OR = 0.263, $P < 0.001$), cholecystectomy (OR = 0.445, $P < 0.001$), (para)thyroid (OR = 0.212, $P < 0.001$), lymph node dissection (OR = 0.114, $P < 0.001$), and appendectomy (OR = 0.540, $P = 0.002$).

After multivariate analysis, the only independent risk factor for moderate and severe pain (VAS ≥ 4) was younger age (<70 years; OR = 0.606, $P = 0.001$) (Table 2), whereas this multivariate analysis also confirmed that patients undergoing five minor surgeries were significantly less likely to report moderate to severe pain compared with patients undergoing colorectal surgery. These include hernia (OR = 0.349, $P = 0.001$), cholecystectomy (OR = 0.477, $P = 0.002$), (para)thyroid (OR = 0.223, $P < 0.001$), lymph node dissection (OR = 0.128, $P < 0.001$), and appendectomy (OR = 0.534, $P = 0.016$) (Table 2 and Figure 6).

At the end of the hospital stay, the mean satisfaction score was 8.18 ± 1.29.

Discussion

Postoperative pain seemed to be adequately controlled in this unselected cohort of visceral surgery patients within a multimodal pain protocol. Pain scores at mobilization were significantly higher than at rest, and younger patients had a higher risk for insufficient pain control. Patients' satisfaction with postoperative pain control was high.

A few reports detailed pain scores after abdominal surgery; these scores are available for comparison with the findings of the present study. Gebershagen et al. [21] analyzed pain scores during the 24 hours postoperation

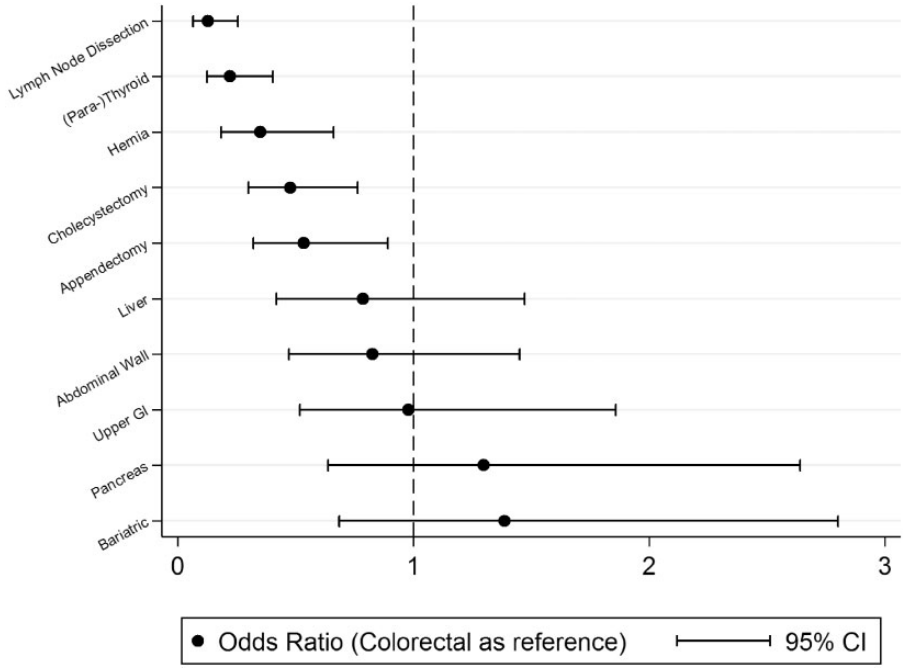

Figure 6. Forest plots illustrating odds ratio of the different types of surgery as independent risk factors for patients reporting moderate or severe pain (visual analog scale ≥ 4). Reference is based on colorectal surgery. CI = confidence interval.

in a large series of diverse surgeries including abdominal procedures. The median pain score for this latter group was 4 in motion, and their highest pain intensity was 5, which is higher than that reported in our present study. They also found pain scores to be higher after minor surgery and theorized that the pain may have been undertreated following minor surgeries compared with major surgeries. In the present study, a lower percentage of patients after minor surgery presented moderate or severe pain at 24 hours and later (Figure 4, Tables 1 and 2) compared with those who had undergone major procedures. However, the present data indicate a high variability of pain scores associated with low morphine equivalent consumption for hernia and (para)thyroid surgeries (Figure 5). This may eventually support the conclusions of Gebershagen et al. that analgesic requirements may be underestimated following minor surgeries.

In our study, patients undergoing bariatric surgery reported the highest pain scores at 24 hours, especially during mobilization (Figures 3 and 4). A paucity of evidence-based recommendations was found in the literature to manage analgesia for this particular type of surgery. Multimodal techniques including regional therapy, avoidance of sedatives, and early mobilization may be key considerations for optimal postoperative care [19, 24]. In the present cohort, intraoperative analgesia was performed using intravenous lidocaine and fentanyl, followed by remifentanil and morphine in the recovery room. Moreover, strong opioids were switched to tramadol due to the increased risk of obstructive sleep apnea [25]. As such, pain score peaks at 24 hours might be a consequence of this strategy. Therefore, prevention of postoperative pain using multimodal intraoperative treatment should be improved [26]. Potential alternatives, however controversial, include TAP block [27, 28], local infiltration at a trocar site [28, 29], or a low dose of intravenous ketamine [30].

From 24 hours to 96 hours, the present data show variant curves of pain scores over time (Figures 2 and 3). All surgeries included, after 24 hours, the curve was rather flat, and this could support the findings of Chapman et al. that 37% of the general population presented a nondecrease of pain scores over time [31]. Generally, we would expect a slow decrease of pain over time; however, probably due to the low mean VAS at rest and during mobilization (Figure 2), lower pain scores were difficult to assess, and the curve appeared flat after 24 hours. Specifically for liver and pancreas surgeries, the curve tended to increase (Figure 3), along with the percentage of moderate and severe pain (Figure 4b), and the explanation could be the withdrawal of epidural catheters at 72 hours, followed by insufficient bridging analgesics. In addition, among patients who underwent cholecystectomy and hernia, there was an increase of moderate and severe pain reported after 24 hours, which coincides with the first mobilization. Although the mean VAS pain score remained relatively low, pain control at patient discharge occurring usually at 48 hours should be improved. A preoperative multimodal therapy for hernia and cholecystectomy using wound infiltration could be considered to extend analgesia, even if the quality of the evidence is limited [32]. Other studies have suggested that TAP block may be more efficient in decreasing pain scores and morphine consumption until 48 hours [33] and could be

Table 2. Multivariate model of all factors with univariate *P* values <0.200

Factor for VAS ≥4	OR	95% CI	*P* Value
Gender			
Female	1 (ref)		
Male	0.846	0.658 to 1.087	0.192
Age, y			
<70	1 (ref)		
≥70	0.606	0.449 to 0.819	0.001
ASA			
I–II	1 (ref)	0.808 to 1.523	0.520
III–IV	1.109		
Surgery type			
Colorectal	1 (ref)		
Bariatric	1.385	0.684 to 2.801	0.365
Upper GI	0.980	0.516 to 1.858	0.950
Liver	0.785	0.419 to 1.470	0.451
Pancreas	1.297	0.637 to 2.639	0.473
Hernia	0.349	0.185 to 0.659	0.001
Cholecystectomy	0.477	0.298 to 0.762	0.002
Abdominal wall	0.826	0.470 to 1.450	0.506
(Para)thyroid	0.222	0.123 to 0.402	< 0.001
Lymph node dissection	0.128	0.064 to 0.255	< 0.001
Appendectomy	0.534	0.320 to 0.890	0.016
Surgery duration			
<180 min	1 (ref)		
>180 min	1.182	0.581 to 2.407	0.643
Anesthesia duration			
<220 min	1 (ref)		
>220 min	1.161	0.555 to 2.428	0.691
Surgical approach (intention-to-treat)			
Open	1 (ref)		
Min. invas./converted	1.057	0.691 to 1.617	0.798
Epidural anesthesia			
No	1 (ref)		
Yes	1.153	0.709 to 1.875	0.566
Lidocaine			
No	1 (ref)		
Yes	1.014	0.646 to 1.593	0.950
Ketamine			
No	1 (ref)		
Yes	0.922	0.490 to 1.735	0.802

Illustration of different independent factors presenting moderate and severe pain (VAS ≥ 4) with a univariate *P* value of <0.200 (Table 1).

ASA = American Society of Anesthesiologists; CI = confidence interval; GI = gastrointestinal; OR = odds ratio; VAS = visual analog scale.

an additive treatment for patients at risk of acute postoperative pain at 48 hours (i.e., hernia repair) and a reasonable alternative treatment in terms of safety and morbidity for patients who undergo a major open or laparoscopic surgery. More recently, some studies have compared bilateral TAP block with epidural analgesia [34, 35] for colorectal surgery by reporting similar effects on pain when applied up to 72 hours postoperatively, with a higher satisfaction score and a shorter time of bladder catheterization in favor of the TAP block.

In our hospital, patients benefit from standardized care maps for most procedures (ERAS and non-ERAS), which allow close pain follow-up [20]. Standard treatment includes paracetamol + novamisulfon or NSAIDs, which is associated with a decrease in pain scores and opioid requirements [36]. Sc morphine or oral oxycodone are prescribed as needed for minor and major surgeries, accompanied by epidural anesthesia for most open major procedures. Interestingly, a heterogeneity of pain management strategies was revealed despite standardized treatment protocols. Potential explanations include, apart from deviations from the protocol due to comorbidities, clinicians' preferences within a multimodal pathway. In-depth evaluation of the impact of protocol deviations on pain control was not possible in the setting of this study. However, this should be a focus of future studies to improve multimodal pain management within ERAS protocols. Systematic introduction of an opioid before first mobilization could be an efficient therapeutic alternative but would need to be carefully monitored in terms of risk of dependency and addiction, specifically in the younger patients [37]. Risk factors for acute postoperative pain have been studied in recent publications, suggesting preoperative chronic pain, young age, and female gender as predominant risk factors [38]. For gender, genetics and hormonal explanations have already been hypothesized, as well as sociocultural differences in pain experience [39]. Many studies have already described higher postoperative pain scores coupled with higher morphine consumption in women [40, 41]. In the present study, no significant difference in gender was observed. Moreover, the present data are consistent with a recent study reporting no difference in pain scores by gender after major abdominal surgery [42]. The reasons might be that the median age was higher in both studies reporting no gender difference than in the one that did report a gender difference. This could explain the differences in pain scores and morphine consumption due to hormonal factors [43]. In line with these explanations, high pain scores were predominantly observed in young patients. One explanation might be the influence of gonadal steroid hormone production on pain perception [43]. Consequently, preventive analgesia for the younger population would be an interesting option: Gabapentin is nowadays commonly used. It reduces morphine and pain score at 24 hours and decreases preoperative anxiety and postoperative nausea, but increases sedation [44]. At low doses (maximum 600 mg preoperatively), it could therefore be useful in younger patients without many side effects. Another alternative might be pregabalin at low doses (≤75 mg preoperatively) [45]. In addition to intravenous lidocaine [13, 46] and ketamine [47, 48], which we usually utilize for major laparoscopic abdominal surgeries, infiltration of local anesthetic, administration of NSAIDs, and epidural anesthesia can be used in a preemptive fashion before incision, which has been shown to reduce VAS pain scores at 24 hours and 48 hours and increase the time to the first rescue analgesic [49]. The timing of each drug still needs to be better defined. Consequently, these treatments should not be employed for all patients and surgeries but specifically according to the type and duration of surgery and the type of patients

in order to improve postoperative care and provide treatment to the patients who will benefit the most of it.

The present study has some limitations. The study cohort was heterogeneous and included a variety of procedures in a single institution. The present data may not be generalizable to other settings. Further limitations were multiple comparative groups, nonuniform pain strategy (potentially leading to selection bias due to subjective pain management preference), and subjective (and partially nonvalidated) end points (satisfaction scale). The history of each patient with respect to preexisting conditions of possible preoperative pain was not systematically reported. Potential confounders such as preoperative patient baseline pain scores and social habits (including smoking) were not systematically collected and thus were not included for further analysis. The duration of the study was determined up to 96 hours and was defined to cover the hospitalization of most minor and major procedures. However, some patients included in the study were discharged before the 96 hours, and the majority who underwent a major surgery stayed longer than four days. An observation until two weeks may have shown additional results or trends in terms of pain score and medication consumption. Moreover, no follow-up was done at a distance to look at the direct complications of our treatment (opioid side effects, infections, or nerve injury after neuraxial anesthesia) and at the potential for chronic postoperative pain onset or opioid dependency. Conversely, there is significant value in reporting on this cohort of >1,000 consecutive, nonselected patients, providing a "real-world" picture of acute postoperative pain in the four days after abdominal surgery.

Conclusions

The present study suggests that our pathways and protocols provide effective pain control after visceral surgery for most patients by use of a multimodal approach, leading to high patient satisfaction. Special attention is needed, however, to improve pain control in younger patients, particularly at mobilization.

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Supplementary Data

Supplementary data are available at *Pain Medicine* online.

References

1. American Society of Anesthesiologists Task Force on Acute Pain Management. Practice guidelines for acute pain management in the perioperative setting: An updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. Anesthesiology 2012;116(2):248–73.
2. Lassen K, Soop M, Nygren J, et al. Consensus review of optimal perioperative care in colorectal surgery: Enhanced Recovery After Surgery (ERAS) group recommendations. Arch Surg Chic Ill 1960 2009;144 (10):961–9.
3. Muller S, Zalunardo MP, Hubner M, Clavien PA, Demartines N; Zurich Fast Track Study Group. A fast-track program reduces complications and length of hospital stay after open colonic surgery. Gastroenterology 2009;136(3):842–7.
4. Vlug MS, Wind J, Hollmann MW, et al. Laparoscopy in combination with fast track multimodal management is the best perioperative strategy in patients undergoing colonic surgery: A randomized clinical trial (LAFA-study). Ann Surg 2011;254(6):868–75.
5. Greco M, Capretti G, Beretta L, Gemma M, Pecorelli N, Braga M. Enhanced recovery program in colorectal surgery: A meta-analysis of randomized controlled trials. World J Surg 2014;38(6):1531–41.
6. Tan M, Law L-C, Gan TJ. Optimizing pain management to facilitate Enhanced Recovery After Surgery pathways. Can J Anaesth J Can Anesth 2015;62 (2):203–18.
7. Koppert W, Schmelz M. The impact of opioid-induced hyperalgesia for postoperative pain. Best Pract Res Clin Anaesthesiol 2007;21(1):65–83.
8. Prabhakar A, Mancuso KF, Owen CP, et al. Perioperative analgesia outcomes and strategies. Best Pract Res Clin Anaesthesiol 2014;28(2):105–15.
9. Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of postoperative pain: A clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain off J Am Pain Soc 2016; 17(2):131–57.
10. Grass F, Cachemaille M, Blanc C, et al. Is standardized care feasible in the emergency setting? A case matched analysis of patients undergoing laparoscopic cholecystectomy. BMC Surg 2016;16(1):78–84.
11. Hübner M, Cerantola Y, Grass F, Bertrand PC, Schäfer M, Demartines N. Preoperative immunonutrition in patients at nutritional risk: Results of a double-blinded randomized clinical trial. Eur J Clin Nutr 2012;66(7):850–5.
12. Berti M, Baciarello M, Troglio R, Fanelli G. Clinical uses of low-dose ketamine in patients undergoing surgery. Curr Drug Targets 2009;10(8):707–15.

13. Kranke P, Jokinen J, Pace NL, et al. Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery. Cochrane Database Syst Rev 2015;7:CD009642.
14. Gustafsson UO, Scott MJ, Schwenk W, et al. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS(®)) Society recommendations. World J Surg 2013;37 (2):259–84.
15. Mortensen K, Nilsson M, Slim K, et al. Consensus guidelines for enhanced recovery after gastrectomy: Enhanced Recovery After Surgery (ERAS®) Society recommendations. Br J Surg 2014;101(10):1209–29.
16. Feldheiser A, Aziz O, Baldini G, et al. Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 2: Consensus statement for anaesthesia practice. Acta Anaesthesiol Scand 2016;60(3):289–334.
17. Melloul E, Hübner M, Scott M, et al. Guidelines for perioperative care for liver surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations. World J Surg 2016;40(10):2425–40.
18. Lassen K, Coolsen MME, Slim K, et al. Guidelines for perioperative care for pancreaticoduodenectomy: Enhanced Recovery After Surgery (ERAS®) Society recommendations. Clin Nutr Edinb Scotl 2012;31 (6):817–30.
19. Thorell A, MacCormick AD, Awad S, et al. Guidelines for perioperative care in bariatric surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations. World J Surg 2016;40(9):2065–83.
20. Page AJ, Gani F, Crowley KT, et al. Patient outcomes and provider perceptions following implementation of a standardized perioperative care pathway for open liver resection. Br J Surg 2016;103(5):564–71.
21. Gerbershagen HJ, Aduckathil S, van Wijck AJM, Peelen LM, Kalkman CJ, Meissner W. Pain intensity on the first day after surgery: A prospective cohort study comparing 179 surgical procedures. Anesthesiology 2013;118(4):934–44.
22. Alschuler KN, Jensen MP, Ehde DM. Defining mild, moderate, and severe pain in persons with multiple sclerosis. Pain Med 2012;13(10):1358–65.
23. Roulin D, Donadini A, Gander S, et al. Cost-effectiveness of the implementation of an enhanced recovery protocol for colorectal surgery. Br J Surg 2013;100 (8):1108–14.
24. Schug SA, Raymann A. Postoperative pain management of the obese patient. Best Pract Res Clin Anaesthesiol 2011;25(1):73–81.
25. Doufas AG, Tian L, Padrez KA, et al. Experimental pain and opioid analgesia in volunteers at high risk for obstructive sleep apnea. PloS One 2013;8 (1):e54807.
26. Andersen LPH, Werner MU, Rosenberg J, Gögenur I. Analgesic treatment in laparoscopic gastric bypass surgery: A systematic review of randomized trials. Obes Surg 2014;24(3):462–70.
27. Sinha A, Jayaraman L, Punhani D. Efficacy of ultrasound-guided transversus abdominis plane block after laparoscopic bariatric surgery: A double blind, randomized, controlled study. Obes Surg 2013;23 (4):548–53.
28. Albrecht E, Kirkham KR, Endersby RVW, et al. Ultrasound-guided transversus abdominis plane (TAP) block for laparoscopic gastric-bypass surgery: A prospective randomized controlled double-blinded trial. Obes Surg 2013;23(8):1309–14.
29. Lam KK, Mui WL. Multimodal analgesia model to achieve low postoperative opioid requirement following bariatric surgery. Hong Kong Med J 2016;22 (5):428–34.
30. Hasanein R, El-Sayed W, Nabil N, Elsayed G. The effect of combined remifentanil and low dose ketamine infusion in patients undergoing laparoscopic gastric bypass. Egypt J Anaesth 2011;27(4):255–60.
31. Chapman CR, Donaldson GW, Davis JJ, Bradshaw DH. Improving individual measurement of postoperative pain: The pain trajectory. J Pain 2011;12 (2):257–62.
32. Loizides S, Gurusamy KS, Nagendran M, Rossi M, Guerrini GP, Davidson BR. Wound infiltration with local anaesthetic agents for laparoscopic cholecystectomy. Cochrane Database Syst Rev 2014;(3):CD007049.
33. Abdallah FW, Chan VW, Brull R. Transversus abdominis plane block: A systematic review. Reg Anesth Pain Med 2012;37(2):193–209.
34. Niraj G, Kelkar A, Hart E, et al. Comparison of analgesic efficacy of four-quadrant transversus abdominis plane (TAP) block and continuous posterior TAP analgesia with epidural analgesia in patients undergoing laparoscopic colorectal surgery: An open-label, randomised, non-inferiority trial. Anaesthesia 2014;69 (4):348–55.
35. Ganapathy S, Sondekoppam RV, Terlecki M, Brookes J, Das Adhikary S, Subramanian L. Comparison of efficacy and safety of lateral-to-medial continuous transversus abdominis plane block with thoracic epidural analgesia in patients undergoing abdominal surgery: A randomised, open-label feasibility study. Eur J Anaesthesiol 2015;32(11):797–804.
36. Martinez V, Beloeil H, Marret E, Fletcher D, Ravaud P, Trinquart L. Non-opioid analgesics in adults after major surgery: Systematic review with network meta-analysis of randomized trials. Br J Anaesth 2017;118 (1):22–31.
37. Kelly MA. Current postoperative pain management protocols contribute to the opioid epidemic in the United States. Am J Orthop (Belle Mead NJ) 2015; 44(Suppl 10):S5–8.
38. Gerbershagen HJ, Pogatzki-Zahn E, Aduckathil S, et al. Procedure-specific risk factor analysis for the development of severe postoperative pain. Anesthesiology 2014;120(5):1237–45.

39. Mogil JS. Sex differences in pain and pain inhibition: Multiple explanations of a controversial phenomenon. Nat Rev Neurosci 2012;13(12):859–66.
40. Aubrun F, Salvi N, Coriat P, Riou B. Sex- and age-related differences in morphine requirements for postoperative pain relief. Anesthesiology 2005;103 (1):156–60.
41. Cepeda MS, Carr DB. Women experience more pain and require more morphine than men to achieve a similar degree of analgesia. Anesth Analg 2003;97 (5):1464–8.
42. Theodoraki K, Staikou C, Fassoulaki A. Postoperative pain after major abdominal surgery: Is it gender related? An observational prospective study. Pain Pract 2014;14(7):613–9.
43. Aloisi AM. Gonadal hormones and sex differences in pain reactivity. Clin J Pain 2003;19(3):168–74.
44. Doleman B, Heinink TP, Read DJ, Faleiro RJ, Lund JN, Williams JP. A systematic review and meta-regression analysis of prophylactic gabapentin for postoperative pain. Anaesthesia 2015;70(10):1186–204.
45. Mishriky BM, Waldron NH, Habib AS. Impact of pregabalin on acute and persistent postoperative pain: A systematic review and meta-analysis. Br J Anaesth 2015;114(1):10–31.
46. Weibel S, Jokinen J, Pace NL, et al. Efficacy and safety of intravenous lidocaine for postoperative analgesia and recovery after surgery: A systematic review with trial sequential analysis. Br J Anaesth 2016;116 (6):770–83.
47. Laskowski K, Stirling A, McKay WP, Lim HJ. A systematic review of intravenous ketamine for postoperative analgesia. Can J Anaesth J Can Anesth 2011;58 (10):911–23.
48. Bell RF, Dahl JB, Moore RA, Kalso E. Peri-operative ketamine for acute post-operative pain: A quantitative and qualitative systematic review (Cochrane review). Acta Anaesthesiol Scand 2005;49(10):1405–28.
49. Ong C-S, Lirk P, Seymour RA, Jenkins BJ. The efficacy of preemptive analgesia for acute postoperative pain management: A meta-analysis. Anesth Analg 2005;100(3):757–73.