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Original Article

Postoperative pain investigation under the protocol of enhanced recovery after abdominal surgery: incidence and risk factors

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Abstract: Postoperative pain (PP) is a great obstacle for the application of enhanced recovery after surgery (ERAS) programs. The current study explored incidence and risk factors of PP under the ERAS protocol. From December 2016 to January 2017, this study retrospectively reviewed 80 patients that completed the ERAS program for abdominal surgery. A visual analog scale (VAS) score was applied to evaluate pain perception within the first three postoperative days, with VAS scores ≥5 considered as moderate-to-severe pain. Patients were divided with cumulative VAS>2 and VAS≤2 scores into the pain group and non-pain group, respectively. PP incidence was 63.8%, with 6.3% for moderate-to-severe pain. PP was associated with prolonged hospital stay (5 vs. 3 days, P=0.018) and increased hospital costs ($5,685.3 vs. $3,708.0, P=0.023). Gender (P=0.033) and malignancy (P=0.027) were independent risk factors of PP. PP remains a challenging problem of ERAS. Pain relief measures should be applied for female or malignant patients, aiming to promote enhanced recovery.

Keywords: Abdominal surgery, postoperative pain, enhanced recovery after surgery, analgesics, risk factors, cancer

Introduction

Generally, postoperative pain (PP) results from lesions in tissues or organs generating stimuli perceived as unpleasant and even painful [1]. When nerve stimuli due to lesions, stretching, or compression occur, the feeling of pain may be quite sharp and intolerable. To date, PP remains a tough medical challenge in most surgical fields.

Moderate-to-severe-pain, reported with pain intensity scores ≥5 on a scale of 0-10 [2], cause decreased performance of daily activities and increased need of analgesics. In addition, this unpleasant complication prolongs hospital stays and is considered clinically unacceptable. Incidence of moderate-to-severe-pain in adults is 2-10% after surgery, with opioids as the mainstay of therapy [3].

The enhanced recovery after surgery (ERAS) program is the integrated perioperative application of medical interventions that can promote postoperative recovery [4]. Underlying goals of this approach are to decrease variability in practice, reduce morbidity and intraoperative stress, enhance the rate of recovery, and shorten postoperative length of stay [5]. Currently, numerous surgical fields, especially those involving the abdomen, have successfully applied this program in clinical practice. However, in China, application of the ERAS program is in the initial phase of introduction, with few results of PP on this protocol available [6, 7]. Additionally, the roles of nursing care in PP management remain obscure. It has been reported that pain perception was increased in the ERAS population, compared with the traditional non-ERAS population [8].

The current study investigated incidence of PP, particularly moderate-to-severe-pain, in adult patients participating in the ERAS program. Importantly, this study explored potential predictive factors of PP, aiming to improve nursing care for these specific populations.

Material and methods

Subjects and surgical principles

The current study is a retrospective analysis of a prospectively collected database of abdominal patients, managed with the ERAS protocol, from December 2016 to January 2017. Present researchers carefully reviewed all perioperative data from the database to select eligible patients. The Institutional Review Board approved the study protocol, with written informed consent obtained from all participations before any treatment.

Within the study period, consecutive patients that consented to participate in the ERAS program and received curative surgery for final analysis were included. As mentioned previously [9], this study excluded individuals in need of emergency laparotomies, with diagnosis of advanced stage malignancies, persistent hemodynamic instability, chronic use of opioids or psychotropic drugs, pain preventing participation, and visual, hearing, or communication impairment, as well as intraoperative intercurrence or intensive care required after surgery. Additionally, this study excluded patients younger than 14 years of age.

Generally, patients with gastrointestinal malignancies typically receive general anesthesia for a curative operation, while those with benign disease (hernia, hemorrhoid, anal fistula, etc.) usually receive regional anesthesia, such as infiltrative anesthesia, peripheral nerve block, epidural, and caudal and spinal anesthesia. All included patients underwent open or laparoscopic surgeries based mainly on clinical assessment and individual preference. Minimally invasive surgery (MIS) consists of any surgical procedure performed mainly using laparoscopy or endoscopy. In addition, surgical wounds were classified into three types: clean (type I), clean-contaminated (type II), and contaminated wounds (type III), preceded by the letter "0" to represent MIS wound or lack of superficial incision [10].

Numerical pain scale

The current study utilized a numerical pain scale, also known as the visual analog scale (VAS), to assess the severity of PP. This scale, comprising 11 (range, 0-10) points, with points 0 (zero) and 10 standing for no pain and the worst perceived pain, respectively, allows the measurement of perceived pain intensity by numbers. Residual numbers represent intermediate intensities of PP (1-4 as mild; 5-6 as moderate; 7-10 as severe) [11]. As described previously, moderate-to-severe pain was defined with a VAS score when the patient self-assessed the score in his/her worst moment at a pain intensity ≥5 points [12].

In the center, the nurses were responsible for the daily recording of VAS scores during morning rounds. This was carried out for three consecutive days after surgery. Subsequently, the secretaries repeatedly recorded such scores on postoperative days (PODs) 5, 7, 14, 21, and 28, regardless of whether the patients were discharged. In this study, patients with no more than 2 points of cumulative VAS ($\sum$VAS ≤2) within the first three postoperative days were considered as free of PP (Non-pain group), since a VAS score of 0 for at least one day and of 2 for no more than one day should indicate a lack of PP. Therefore, analgesics were not required for those patients. In contrast, patients with at least 3 cumulative VAS points within the first three postoperative days were considered as suffering from PP (Pain group), with pain relief measures and additional assessments provided.

ERAS protocol of pain management

ERAS protocol consisted of admission education, no bowel preparation, an oral carbohydrate load before surgery, smaller incisions, thermostasis during surgery, avoidance of nasogastric tubes, intra-abdominal drains and urinary drainage after surgery, early ambulation under optimal control of PP, and a quicker recovery of oral intake [4, 13]. In detail, this study primarily used intravenous/oral nonsteroidal anti-inflammatory drugs (NSAIDs) to control PP, employing an epidural catheter to infuse a constant rate of local anesthetics for more consistent pain. Notably, additional analgesia was not administered unless the VAS score was greater than 3 points, with intravenous morphine and secondary oral opioids applied as breakthrough pain medications. Routinely, pain-relief measures were stopped at POD 4, unless otherwise indicated. Thus, most patients were off analgesics at the time of oral refeeding in the hospital and preferred using nonopioid drugs if required.

Primary and secondary outcomes

The primary outcome was overall incidence of PP, including moderate-to-severe pain, under the current ERAS protocol. Secondary outcomes included unpleasant events after surgery, postoperative length of stay (LOS), incidence of postoperative complications, and hospital costs, except for surgical expenses.

To further explore predictive factors of postoperative pain, this study intentionally divided included patients into two groups, the pain group and non-pain group, as described above. Using multivariate logistic regression analysis, this study detected some predictive factors of PP from several clinical factors, such as age, gender, body mass index (BMI), comorbidities, American Society of Anesthesia (ASA) scores, operative duration, regional use of analgesics, types of anesthesia, and incisional wounds.

Statistical analysis

Descriptive statistics were used to present demographics and outcomes, with mean ± standard deviation (SD) for continuous variables, counts plus proportion for categorical variables, and medians with range values for non-normally distributed data. Kruskal Wallis ANOVA and a Chi-Squared tests were employed to compare continuous variables and percentages between the two groups, respectively. Using a multivariate logistic regression model, this study investigated potential risk factors for postoperative pain. Notably, some exposition variables included in this model presented a *P* value ≤0.10, according to univariate analysis. Data analyses were performed using IBM SPSS (Ver. 23.0; Chicago, IL, USA). All tests were two-tailed and *P* values <0.05 (two-sided) indicate statistical significance.

Results

General features of enrolled subjects

Within the study period, a total of 80 patients were included for final analysis. Median age was 54 (range, 17-84) years, with 51 (63.8%) male patients enrolled. Median BMI was 22.1 (range, 15.4-31.6) kg/m^2 in this cohort, with only one participant suffering from severe comorbidity. As mentioned above, patients were assigned to pain and non-pain groups, according to cumulative VAS scores within the first three postoperative days. Demographic and baseline features of the study population are summarized in **Table 1**. Comparisons between the two groups indicated that gender and malignancy were significantly different (P<0.05), whereas age, BMI, ASA, comorbidity, and perioperative measures were similar (P>0.05). Notably, operative duration in the pain group was relatively prolonged, compared with that in the non-pain group (median, 112 vs. 95 min; P= 0.153).

Postoperative pain incidence and short-term outcomes

In this study, 49 (61.2%) patients had undergone nonmalignant surgeries, with tension-free inguinal herniorrhaphy most frequently performed in 35 (71.4%) of 49 patients. PP incidence was markedly reduced after nonmalignant surgery, compared with that after malignant tumor resection (40.8% vs. 67.7%, P= 0.023). Overall, average VAS scores were 1.8± 1.7 (range, 0-7) at POD 1, 1.3±1.1 (range, 0-3) at POD 2, and 1.2±1.1 (range, 0-3) at POD 3. The maximal VAS score for this cohort was 7 points in only one case (1.3%), with 0 point recorded in 29 cases (36.2%). Hence, PP incidence was 63.8% in the current study population. Specifically, incidence of moderate-to-severe pain was 6.3%, with only one subject having severe pain at POD 2. Postoperative analgesics were applied for 31 (38.7%) patients. However, it is noteworthy that the clinical usage of analgesics was similar between pain and non-pain groups (P=0.059). Notably, NSAID analgesics were used more frequently than opioid drugs for PP control (36.3% vs. 5.0%, P=0.027). In addition, it was found that local or continuous intravenous analgesics failed to improve pain control in this cohort (**Table 2**). Despite pain complaints, this study recorded other unpleasant complaints in 23 (28.8%) patients, including nausea in seven cases, sleep reduction in five cases, abdominal distention in six cases, vomiting in four cases, and urinary retention in three cases.

Median LOS in the hospital was 6 (range, 2-36) days. This time was relatively prolonged in the pain group, compared with that in the non-pain group (9 vs. 5 days, P=0.080). However, median postoperative LOS was markedly increased (5 vs. 3 days, P=0.018). Additionally, both total

Table 1. Demographic and baseline characteristics of patients under the ERAS protocol

	The Pooled (n=80)	Pain group (n=41)	Non-pain group (n=39)	*P* value
Age, yrs.	52.8±22.3	51.7±18.6	52.8±22.6	0.776
Gender, male (%)	51 (63.8)	21 (51.2)	30 (76.9)	0.021
BMI, kg/m^2	22.3±3.2	22.0±3.7	22.6±2.4	0.401
ASA, n (%)				0.610
I+II	79 (98.8)	40 (97.5)	39 (100)	
≥III	1 (1.2)	1 (2.4)	0	
Malignancy, n (%)	31 (38.8)	21 (51.2)	10 (25.6)	0.023
Gastric cancer	7 (8.7)	5 (12.2)	2 (5.1)	
Colorectal cancer	17 (21.3)	12 (29.3)	5 (12.8)	
Others	7 (8.7)	4 (9.7)	3 (7.7)	
Comorbidity, n (%)				
DM	4 (5.0)	2 (4.9)	2 (5.1)	0.673
HTN	12 (15.0)	6 (14.6)	6 (15.4)	0.586
Alcohol addiction, n (%)	6 (7.5)	3 (7.3)	3 (7.7)	0.722
Anesthesia measure, n (%)				0.121
Local An.	2 (2.5)	0	2 (5.1)	
Spinal An.	3 (3.8)	0	3 (7.7)	
Caudal An.	1 (1.3)	0	1 (2.6)	
Epidural An.	20 (25.0)	10 (24.4)	10 (25.6)	
Endotracheal An.	6 (7.5)	2 (4.9)	4 (10.3)	
General An.	48 (60.0)	29 (70.7)	19 (48.7)	
MIS, n (%)	25 (31.3)	14 (34.1)	11 (28.2)	0.634
Wound Type, n (%)				0.756
I/OI	37 (46.3)	18 (43.9)	19 (48.7)	
II/OII	34 (42.5)	19 (46.3)	15 (38.5)	
III	9 (11.3)	4 (9.8)	5 (12.8)	
Operative time, min	135.0±101.6	150.9±114.0	118.3±84.9	0.153

Patients were divided into two groups, as mentioned above, for comparison. Data are presented as the means ± SD or count (percentage of column). Abbreviations: BMI, body mass index; ASA, American society of anesthesia; DM, diabetes mellitus; HTN, hypertension; An., anesthesia; MIS, minimally invasive surgery. P<0.05 indicates significance between the two groups.

hospital costs and operation-free costs were significantly higher in the pain group than in the non-pain group (**Table 2**). Moreover, surgical expenses were also significantly different between the two groups ($397.4±247.1 vs. $291.1±151.2, P=0.026). However, incidence of postoperative complications was not significantly different between the two groups, with only one case of wound infection observed. Notably, no patients suffered persistent PP within a month of follow-up.

Risk factors of postoperative pain

Using logistic regression analysis, it was found that gender (P=0.033) and malignancy (P=0.027) were independent predictive factors of PP for patients participating in the ERAS program (**Table 3**). Specifically, female patients with resectable malignancies would more likely suffer from pain after surgery. However, other factors, such as older age, increased BMI, or complicated surgery, were not linked to PP in the current study.

Discussion

This retrospective study reviewed patients participating in the ERAS program, aiming to investigate incidence and risk factors of PP. Present results indicate that PP incidence under the ERAS protocol was 63.7%, particularly 6.3% for moderate-to-severe pain. In addition, current findings suggest that the female gender and malignancies were independent predictive factors of PP for current study populations.

Table 2. Pain management and short-term outcomes under the ERAS protocol

	The Pooled (n=80)	Pain group (n=41)	Non-pain group (n=39)	*P* value
Local analgesics, n (%)	2 (2.5)	2 (4.9)	0	0.494
Analgesic pump[a], n (%)	21 (26.6)	14 (34.1)	7 (18.4)	0.133
VAS[b], point				<0.001
POD 1	2 (0-7)	3 (2-7)	0 (0-2)	
POD 2	2 (0-3)	2 (2-3)	0 (0-2)	
POD 3	2 (0-3)	2 (0-3)	0 (0-2)	
Maximal pain intensity, n (%)				<0.001
No pain (0)	29 (36.2)	0	29 (74.4)	
Mild (1-4)	46 (57.5)	36 (87.8)	10 (25.6)	
Moderate (5-6)	4 (5.0)	4 (9.8)	0	
Severe (7-10)	1 (1.3)	1 (2.4)	0	
Postop. analgesics				0.059
NSAIDs	29 (36.3)	18 (43.9)	11 (28.2)	
Opioids	4 (5.0)	4 (9.8)	0	
None	49 (61.3)	21 (51.2)	28 (71.8)	
LOS[b], day	6 (2-36)	9 (2-36)	5 (2-21)	0.080
Postop. LOS[b], day	3 (1-28)	5 (2-28)	3 (1-10)	0.018
Postop. complications[c], n (%)	1 (1.3)	1 (2.4)	0	0.513
Reoperation	0	0	0	
Non-surgery	1 (1.3)	1 (2.4)	0	
Hospital cost, *dollar*	4,721.5±3,937.0	5,685.3±4,729.3	3,708.0±2,573.8	0.023
Non-surgery cost, *dollar*	4,375.8±3,766.2	5,287.9±4,526.4	3,416.9±2,466.2	0.024

[a]One participant missing. [b]The data are presented as the median (range). [c]We managed patients with postoperative complications using planned reoperation or conservative measures. NOTE: VAS, visual analog scale; POD, postoperative day; Postop., postoperative; NSAIDS, nonsteroidal anti-inflammatory drugs; LOS, length of stay; P<0.05 indicates a significant difference between the pain and non-pain groups.

Table 3. Predictive factors of postoperative pain under the ERAS protocol

Factor	B	*P* value	HR	95.0% CIs HR	
				Lower	Upper
Age	-0.730	0.2180	0.482	0.118	1.970
Gender	1.412	*0.033*	4.103	1.107	15.209
BMI	-0.167	0.740	0.846	0.314	2.275
Malignancy	-2.122	*0.027*	0.120	0.018	0.816
DM	-0.636	0.625	0.530	0.041	6.773
HTN	1.206	0.179	3.341	0.575	19.418
Anesthesia measures	0.382	0.297	1.465	0.715	3.001
ASA	0.213	0.774	0.238	0.288	5.230
Operative difficulty	0.509	0.344	1.664	0.579	4.778
Wound type	0.647	0.213	1.910	0.689	5.294
Minimally invasive surgery	-0.168	0.808	0.845	0.217	3.297
Local analgesics	-10.761	0.878	-	-	-
Operative duration	0.833	0.359	2.301	0.388	13.654

Multivariate logistic regression was used with the enter method for risk factor prediction. The cut-off values for each factor were as follows: Age, 65 yrs.; Gender, Male; BMI, 25.5 kg/m^2; ASA, I+II vs. ≥III; Operative difficulty, I+II vs. III+IV; Wound type, I+OI vs. others; Operative duration, 180 min; P<0.05 indicates an independent association with postoperative pain. Abbreviations: B, slope of regression; HR, hazard ratio; CIs, confidential intervals; BMI, body mass index; DM, diabetes mellitus; HTN, hypertension; ASA, American society of anesthesia.

Pain relief after surgery remains a major medical challenge. However, recent surveys from the US and Europe do not show any exciting progress in pain management [14, 15]. A 2011 report from the US showed that more than 80% of surgical patients suffer from PP, with fewer than 50% receiving adequate pain management [16]. Before the introduction of the ERAS program, opioid monotherapy remained the foundation of PP management. A recent retrospective review based on more than 300,000 patients across 380 US hospitals showed that approximately 95% of surgical patients receive opioids to treat PP [17]. However, opioids have several

dose-limiting side effects, ranging from tiny and unpleasant to life-threatening. These include nausea, vomiting, constipation, ileus, over-sedation, and respiratory depression. To date, multimodal analgesia, including local analgesics, epidural anesthesia, NSAIDs, opioids, or intravenous morphine patient-controlled anesthesia, has gained much popularity in an increasing number of surgical fields.

The ERAS protocol is designed to reduce perioperative stress and promote postoperative recovery. The success of ERAS depends on the complete fulfillment of this protocol. Peri-anesthesia nurses are an important part of this achievement [18]. In clinical practice, nurses are mainly responsible for advocating the ERAS protocol to surgical patients, including basic care during hospital stays, stoma care education, pain self-assessment education, assistance with prescriptions, and necessary contact after hospital discharge. In fact, contrary to popular belief, the implementation of such a protocol may decrease nursing workloads per patient because a standardized workflow could improve the efficiency of daily care and reduce errors.

A cornerstone of nursing care under the ERAS protocol is early notice of patient needs and any unpleasant feelings [19]. More precise nursing care, in collaboration with the surgeon, may improve the perioperative management of surgical patients, especially for PP management. A previous study showed that incidence of moderate-to-severe pain in ERAS patients was significantly lower and approximately one-third of that in traditional cases (7.3% vs. 22%) [20]. The 6.3% incidence rate in the current study is comparable to that reported in previous studies. In addition, present findings indicate a lower VAS score (mean, 1.4) and shorter postoperative LOS (median, 3 days), compared with that in similar studies [4, 21, 22].

Limitations of this study stem from the retrospective design. First, although the ERAS protocol was fully implemented, preoperative anxiety for each patient was not evaluated. Hence, it was possible to amplify or conceal PP incidence in the current cohort. The so-called "work of worry" theory has confirmed the relationship between anxiety and PP by numerous surgical procedures [23-26]. Second, the relatively small sample size may decrease the power of present findings, with limited risk factors found. The enrollment of more patients and external subgroup analyses are required to validate these findings. Finally, a strict prospective study with a randomized controlled design is required to further confirm the roles of the ERAS program in pain relief for abdominal patients.

Under the ERAS program, 63.7% of abdominal patients still had some degree of postoperative pain. Although a low incidence of moderate-severe pain was achieved via the ERAS protocol, more pain relief measures, along with precise nursing care, should be applied for female or malignant patients, aiming to promote better recovery after abdominal surgery.

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Disclosure of conflict of interest

None.

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