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ORIGINAL RESEARCH

Factors influencing length of hospital stay in patients using patient-controlled analgesia after laparotomy surgery-retrospective observational study

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Abstract

Multiple factors influencing the length of hospital stay (LOS) were investigated in patients using patient-controlled analgesia (PCA) after surgical laparotomy for various abdominal pathologies. Charts of patients who underwent fentanyl-based PCA for pain control after different types of exploratory laparotomy were reviewed retrospectively between January and December of 2014. Data from the preoperative, perioperative, and postoperative period were statistically analyzed using the Pearson's correlation coefficient (PCC) and a multiple linear regression in relation to LOS. In the subgroup analysis, a significant positive correlation was found between an increased PCA-fentanyl dosage (μg/kg) and LOS in the gynecologic laparotomy-cancer (GyLC) group (PCC = 0.408; $p < 0.05$). In contrast, the PCA-fentanyl high dose (>500 μg/day) had a significant negative correlation with LOS in the general surgery-laparotomy-liver transplant-donor (GLLTD) group (PCC = −0.402; $p < 0.05$). Factors such as American Society of Anesthesiologists (ASA) classification, diabetes mellitus, hypertension, chronic kidney disease, age, surgical time, perioperative total fluid/urine/blood loss, blood transfusion, use of tetrastarch, vomit/pruritus during PCA use, and total amount of fentanyl use were demonstrated to be positively correlated with LOS in the various groups of patients. Only blood transfusion was a predictive variable for prolonged LOS in GyLC group. Chronic kidney disease, total perioperative fluid, and vomiting during PCA use were predictive of LOS in the gynecologic laparotomy-non-cancer (GyLNC) group. There are multiple factors that affect LOS in patients using PCA after laparotomy for various surgical procedures. Acute pain physicians should take the clinical situation into consideration when prescribing the postoperative opioid-PCA dosage.

Keywords

Postoperative pain; Fentanyl; Opioid; Side effects; Recovery

1. Introduction

Postoperative pain management has remained one of the most delicate medical issues in recent decades. In spite of increased attention to postoperative pain treatment, over 80% of surgical patients still experience postsurgical pain [1]; 12% of patients still experience "severe-to-extreme" pain and 54% have "moderate-to-extreme" pain [2]. Inadequate post-surgical pain control may restrict patient mobilization as well as respiratory function, in turn causing thromboembolic events and lung atelectasis and/or pneumonia [3], even leading to the development of prolong chronic pain [4].

Surgical laparotomy is a procedure used to examine the abdominal organs for any abnormality. The extent of exploratory laparotomy varies from a simple appendectomy to more complicated procedures such as tumor resection, hepatectomy, or liver transplantation, depending on how complex the abdominal pathology is and the magnitude of the surgical injury that is involved in the procedure. Theoretically, a more complicated laparotomy involves more tissue damage and further inflammation reactions that require more extensive postoperative care, as well as pain control [5, 6].

Intravenous opioid patient-controlled analgesia (PCA) is a useful tool for the management of post-surgical acute pain [7, 8]. The advantages of this modality include a conscious patient can activate the system and self-administer a set dose of opioid for pain relief easily without waiting for a caregiver, and a therapeutic serum level based on the varied analgesic needs of each patient can be maintained while minimizing the side effects [7, 8]. PCA offers many potential benefits, including higher patient satisfaction due to better postoperative analgesia and decreased risk of postoperative pulmonary complications, compared to conventional pro re nata (PRN) analgesic regimens [7, 9]. Although opioid monotherapy still

has the general basis of postsurgical pain control [1], the use of restrictive opioids together with multimodal postoperative pain therapy have recently been advocated based on a new concept of enhanced recovery after surgery (ERAS), due to concerns of increased incidence of opioid-induced postoperative ileus as well as many other common side effects [10, 11]. Consequently, determining how to wisely prescribe an appropriate amount of opioids for a given surgical procedure or individual to avoid or minimize the increases in LOS should be the first prioritized concern of every acute pain management physician.

Therefore, we evaluated multiple factors that would influence the length of hospital stay (LOS) for patients using intravenous opioid PCA after laparotomy in gynecologic and general surgery.

2. Methods

This study was conducted in a tertiary medical center of Southern Taiwan from January to December in 2014. All methods were performed in accordance with relevant guidelines and regulations.

Electronic medical records of 1088 patients using fentanyl-based patient-controlled analgesia (PCA) after surgery for pain control were reviewed retrospectively. The exclusion criteria included cases with missing data, surgical procedures other than laparotomy of general and gynecologic surgery, age under 20 years old, and anesthesia methods other than intubated general anesthesia.

Data from the preoperative, perioperative, and postoperative periods of each enrolled patient were collected. The basic demographic characteristics of the patients included gender, age, body mass index (BMI), American Society of Anesthesiologists (ASA) physical status classification, preoperative hemoglobin, and co-morbidities (diabetes mellitus, hypertension, cerebral vascular disease, coronary artery disease, chronic kidney disease, and end-stage renal disease). In the perioperative period, surgery duration, perioperative opioid dosage equivalent to fentanyl, amount of urine output, intravenous fluid, blood loss, blood transfusion, and use of tetrastarch were collected. In the postoperative period, PCA-related factors such as the numerical pain scale (NRS, 0 = no pain; 10 = worst pain) were registered during rest and movement of the first visit, the dosage of fentanyl (μg) used (perioperative plus postoperative PCA; all analgesics were recalculated and recorded according to fentanyl equivalent dose as ratio of fentanyl:morphine = 100:1, fentanyl:alfentanyl = 10:1, fentanyl:pethidine = 1000:1), and the side effects (nausea, vomiting, pruritus, abdomen fullness) were registered. The post-operative length of hospital stay (LOS), which was set as the endpoint of the study, was also recorded.

Patients who had undergone a laparotomy with the use of postoperative PCA in general and gynecologic surgery were enrolled in the study. For a further subgroup analysis, the patients were allocated as follows (Fig. 1): GS (general surgery) laparotomy-liver transplant-recipient (GLLTR), GS laparotomy-liver transplant-donor (GLLTD), GS laparotomy-hepatectomy (GLH), GS laparotomy-other disease (GLO), Gyn (gynecologic) laparotomy-non-cancer (GyLNC), and Gyn laparotomy-cancer (GyLC).

The daily anesthetic practice protocols for patients receiving postoperative PCA were as follow: (1) routine dexamethasone 5–10 mg was given intravenously to all surgical patients without contraindications to the agent; (2) an additional 8 mg of ondansetron was administered intravenously in patients who were classified as medium-to-high risk for postoperative nausea and vomiting (PONV) based on the Apfel score [12, 13].

Statistical analyses were performed using SPSS software ver. 25.0 (IBM, Armonk, NY, USA). Categorical variables were presented as percentage. Data for continuous variables were expressed as mean and standard deviation (SD). The Pearson's correlation coefficient (PCC) analysis was used to evaluate the relationship between multiple variables and length of stay (LOS) among the study population and in the various subgroups. Insignificant variables in the initial analysis of the study population were discarded. Only significant variables were selected for further subgroup analysis. A p value < 0.05 was taken to indicate statistical significance. Finally, multiple linear regression models were performed separately to assess the impact of the independent variables on LOS. Subgroups with at least five significant variables (based on the PCC analysis) were selected for further multiple linear regression analyses.

3. Results

A total of 383 patients using intravenous opioid PCA after laparotomy in gynecological and general surgery were included in this study (Fig. 1). Preoperative, perioperative, and postoperative demographic data are shown in Table 1. The results of the Pearson's correlation coefficient (PCC) of factors affecting the LOS for the study population are shown in Table 2.

3.1 Factors influencing LOS in the study population (Table 2)

Among the preoperative factors, it is found that preoperative hemoglobin levels had a significant negative correlation with LOS (*i.e.*, lower preoperative hemoglobin levels may lead to an increased LOS) (PCC = −0.167; $p < 0.05$). In contrast, the patient's age had a significant positive correlation with LOS (*i.e.*, older patients might have an increased likelihood of a longer LOS) (PCC = 0.22; $p < 0.05$). In addition, diabetes mellitus as well as female gender also had significant positive correlations with LOS (PCC = 0.151 and 0.356, respectively; $p < 0.05$). Among the perioperative factors, we found that surgical time, fentanyl (μg/kg), total intravenous (IV) fluid (mL/kg), total IV fluid (mL/kg/hr), blood transfusion, total urine output (mL/kg/hr and mL/kg), and total blood loss (mL/kg) also had significant positive correlations with LOS (all $p < 0.05$). Finally, factors that demonstrated significant positive correlation with LOS in the postoperative period were pruritus during PCA, PCA-fentanyl (μg/kg), PCA fentanyl (μg/day), PCA-fentanyl low dose (<500 μg/day), PCA-fentanyl (μg/day/kg), PCA-fentanyl low dose (<10 μg/day/kg), PCA-fentanyl (μg/day), PCA-fentanyl low dose (<500 μg/day), total fentanyl (μg/kg),

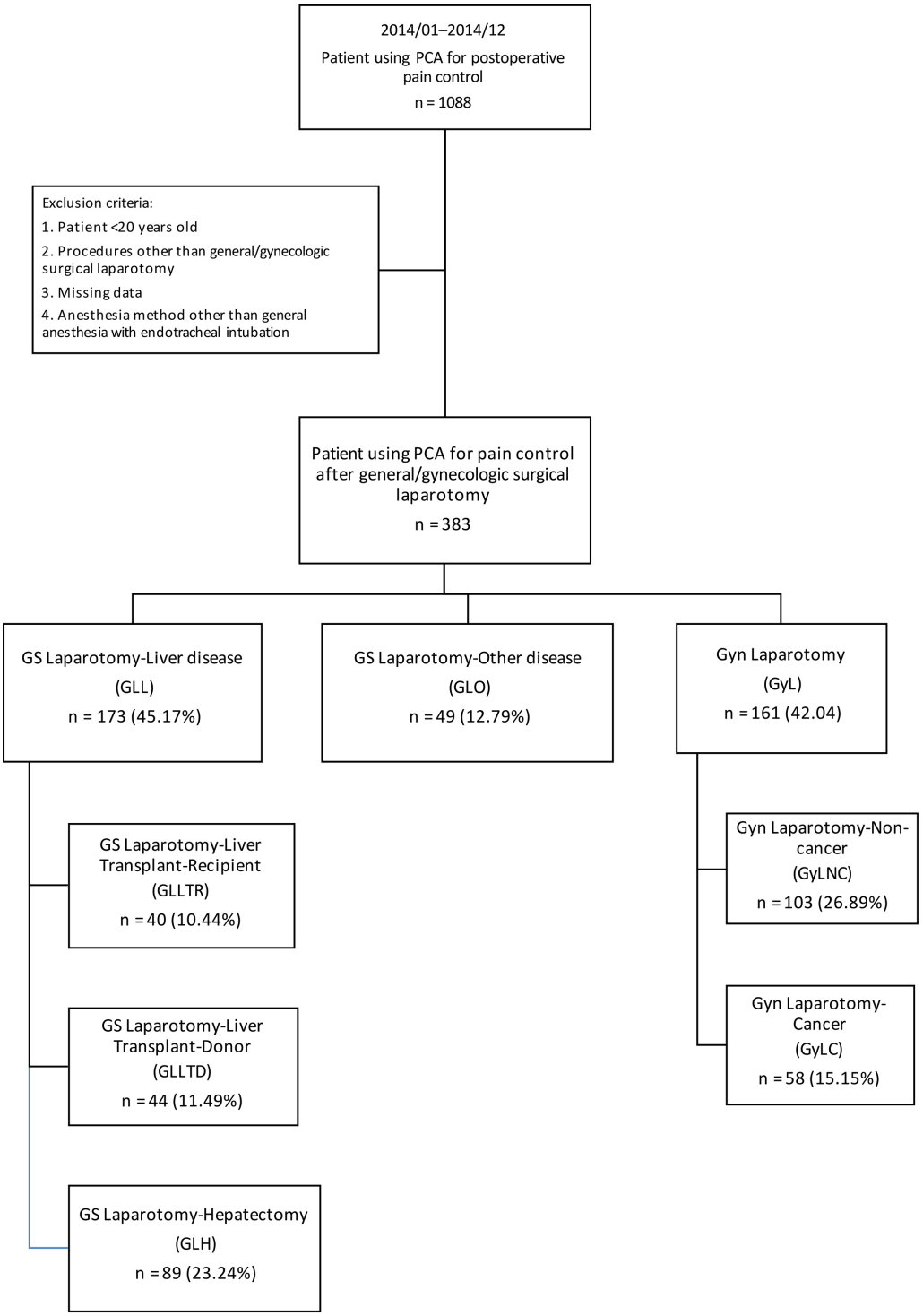

FIGURE 1. Schematic of the patient selection process. PCA: Patient-controlled analgesia.

total fentanyl (μg/day/kg), and total fentanyl (μg/day) (all $p < 0.05$).

3.2 Factors influencing LOS in the subgroup analysis (Table 3)

A subgroup analysis was performed based on the type of exploratory laparotomy in both general and gynecologic surgery (Fig. 1). Among the preoperative factors, the ASA classification and diabetes mellitus were found to be significantly positively correlated with LOS in the GLH group ($p < 0.05$). In addition, hypertension and chronic kidney disease had a positive correlation with LOS in the GLLTR and GyLC groups, respectively ($p < 0.05$). Furthermore, hypertension, chronic kidney disease, and age were positively correlated with LOS in the GyLNC group ($p < 0.05$).

Among the perioperative factors, surgical time and total IV fluid (mL/kg) were positively correlated with LOS in the GLH, GyLNC, and GyLC groups ($p < 0.05$). Besides, total blood loss (mL/kg), use of tetrastarch, and tetrastarch (mL/kg) were also shown to be positively correlated with LOS in GLH group ($p < 0.05$). In addition, total blood loss (mL/kg), blood

transfusion, and tetrastarch (mL/kg) were factors that indicated positive correlation with LOS in the GyLC group ($p < 0.05$) as well. In the GLLTR group, total urine (mL/kg/hr) was the only factor that had a positive correlation with LOS ($p < 0.05$). Furthermore, it is found that total IV fluid (mL/kg/hr) was the only factor that had a significant negative correlation with LOS in the GLLTD group ($p < 0.05$).

Among the postoperative factors, pruritus and vomiting during PCA had a positive correlation with LOS in the GLLTR and GyLNC groups, respectively ($p < 0.05$). Furthermore, PCA-fentanyl (μg/kg), total fentanyl (μg), and total fentanyl (μg/kg) were the factors that also showed positive correlations with LOS in the GyLC group ($p < 0.05$). Interestingly, PCA-fentanyl (μg/day), PCA-fentanyl high dose (>500 μg/day), PCA-fentanyl (μg/day/kg), total fentanyl (μg/day/kg), total fentanyl high dose (>10 μg/day/kg), total fentanyl (μg/day), and total fentanyl high dose (>500 μg/day) were found to have significant negative correlations with LOS in the GLLTD group ($p < 0.05$).

3.3 Multiple linear regression analysis in selected subgroups

Multiple linear regression models were performed separately to assess the impact of the independent variables on LOS. Subgroups with at least five significant variables (based on the PCC analysis) were selected for further multiple linear regression analyses. Blood transfusion was a determining factor having significant impact on prolonged LOS in the GyLC group (B = 7.824 $\pm$ 2.205; p = 0.001) (Table 4.1). In addition, chronic kidney disease (B = 12.693 $\pm$ 5.335; p = 0.019), perioperative total IV fluid (mL/kg) (B = 0.152 $\pm$ 0.055; p = 0.019), and postoperative vomiting during PCA use (B = 5.67 $\pm$ 2.195; p = 0.011) were the three major factors that led to prolonged LOS in the GyLNC group (Table 4.2). Unfortunately, all variables had insignificant results in the GLH group (Table 4.3).

4. Discussion

According to the previous studies, opioid-related adverse drug events are associated with significant increases in LOS in a dose-dependent manner [14–16]. Although the opioid-related adverse effects of PCA in this studied population were identical to those reported in previous studies [14–16], the incidence of PCA-related adverse effects in this study was relatively lower than a previous similar report [17]. In our institution, fentanyl-based IV-PCA is used instead of morphine-based IV-PCA for postoperative pain control because fentanyl is a synthetic opioid, does not induce histamine release [18], has no active metabolites [18], has fewer opioid-related adverse effects than morphine [19], and obtains higher patient satisfaction scores [19]. Another explanation for the low incidence of opioid-related adverse events was that the consensus guidelines for the management of postoperative nausea and vomiting were strictly followed [13]. As a daily anesthetic practice, 5–10 mg of intravenous dexamethasone was routinely given to all surgical patients without contraindications to the agent. Additional 8 mg of ondansetron was administered intravenously in patients who were classified as medium-to-high risk for PONV based on the Apfel score [12].

As expected in this retrospective observational study, there were multiple factors in the preoperative, perioperative, and postoperative periods that influenced the LOS of patients using PCA after exploratory laparotomy, as shown in Table 2. Importantly, we further performed a subgroup analysis to identify the most determinant factors in terms of affecting the LOS of patients with different surgical laparotomy procedures. Interestingly, the results showed an important finding suggesting that the type of exploratory laparotomy was a determinant factor affecting LOS. After a detailed subgroup analysis, a statistically significant positive correlation was found between the amount of opioid use in PCA and LOS in the Gyn laparotomy-cancer (GyLC) group. Among the side effects of intravenous opioid PCA, only pruritus and vomiting had significant positive correlations with LOS in the GS laparotomy-other disease (GLO) group and the Gyn laparotomy-non-cancer (GyLNC) group, respectively.

Interestingly, total blood loss (mL/kg), tetrastarch (mL/kg), and total intravenous fluid (mL/kg) showed significant positive correlations with LOS in the GS laparotomy-hepatectomy (GLH) and Gyn laparotomy-cancer (GyLC) groups. And it was not surprising that tetrastarch and intravenous fluid volume replacement were related to the amount of blood loss. These findings could be explained by the etiology and complexity of cancer in both groups, which might further escalate the difficulty of surgical procedures and increase the amount of blood loss, where the infusion of tetrastarch was necessary to keep perioperative hemodynamics stable and further contributed to the increased LOS. These findings were similar to those of previous reports [20–23], suggesting the importance of perioperative fluid management. Therefore, acute pain physicians should be aware of the patient's perioperative surgical and anesthesia courses or events and take them into clinical consideration when prescribing PCA opioid dosages in order to prevent prolonged LOS for patients undergoing general and gynecologic cancer surgeries.

Among the variables in the subgroup analysis, surgical time was also found to have a significant positive correlation with LOS in the GLH, GyLNC, and GyLC groups. Although the surgical time in the GLO, GLLTR, and GLLTD groups had insignificant PCC results, which might have been due to the small number of patients, they still exhibited a trend toward a positive correlation with LOS. As mentioned above, the complexity of the disease being surgically treated might lead to difficulty of surgical intervention, increased surgical time, perioperative blood loss, and unstable hemodynamics [20–22]. To minimize such deleterious clinical situations, patients should be well prepared with invasive sophisticated hemodynamic monitoring, such as central venous and arterial catheterization, which are time-consuming procedures. It is not surprising that patients who undergo such complicated surgical interventions might have postoperative complications [22] that require more recovery time, hence contributing to prolonged LOS, as expected.

TABLE 1. Demographic data of study population (n = 383).

Preoperative data	
Gender (n/%)	
Female	243 (63.45%)
Male	140 (36.55%)
BMI (mean ± SD)	25.36 ± 13.23
Age (mean ± SD)	50.00 ± 13.17
ASA classification(n/%)	
I	67 (17.49%)
II	207 (54.05%)
III	109 (28.46%)
Hemoglobin level (mg/dL) (mean ± SD)	12.30 ± 2.07
Comorbidity (n/%)	170 (44.39%)
Diabetes mellitus	57 (14.88%)
Coronary artery disease	12 (3.13%)
Hypertension	85 (22.19%)
Cerebrovascular accident	7 (1.83%)
Chronic kidney disease	8 (2.09%)
End-stage renal disease	1 (0.26%)
Number of comorbidities	
1–2 item	373 (97.39%)
>2 item	10 (2.61%)
Perioperative data	
Surgical time (min) (mean ± SD)	297.72 ± 175.29
Fentanyl (μg/kg) (mean ± SD)[§]	2.66 ± 1.27
Total intravenous fluid (mL/kg) (mean ± SD)	650.60 ± 638.62
Total intravenous fluid (mL/kg/hr)	10.55 ± 11.00
Blood transfusion (%)	64 (16.71%)
Use of tetrastarch (%)	40 (10.44%)
Tetrastarch (mL/kg)	0.95 ± 2.86
Total urine output (mL/kg/hr) (mean ± SD)	2.01 ± 2.00
Total urine output (mL/kg) (mean ± SD)	10.11 ± 10.13
Total blood loss (mL/kg) (mean ± SD)	8.38 ± 19.76
Postoperative data	
NRSR 1st visit (mean ± SD)[†]	1.93 ± 1.32
NRSM 1st visit (mean ± SD)[‡]	3.74 ± 1.70
Side effects of PCA (%)	32 (8.36%)
Nausea (%)	17 (4.44%)
Vomit (%)	11 (2.87%)
Pruritus (%)	9 (2.35%)
Abdomen distension (%)	1 (0.26%)
PCA-fentanyl (μg/kg) (mean ± SD)	29.64 ± 23.34
PCA-fentanyl (μg/day/kg) (mean ± SD)	9.97 ± 5.33
PCA-fentanyl low dose (<10 μg/day/kg) (mean ± SD)	6.34 ± 2.39
PCA-fentanyl high dose (>10 μg/day/kg) (mean ± SD)	14.93 ± 4.09
PCA-fentanyl (μg/day) (mean ± SD)	624.10 ± 342.61
PCA-fentanyl low dose (<500 μg/day) (mean ± SD)	318.45 ± 117.40
PCA-fentanyl high dose (>500 μg/day) (mean ± SD)	820.87 ± 291.79
Total fentanyl (μg/kg) (mean ± SD)[#]	32.30 ± 23.72

TABLE 1. Continued.

Preoperative data	
Total fentanyl (μg/day/kg) (mean ± SD)[#]	11.10 ± 5.34
Total fentanyl low dose (<10 μg/day/kg) (mean ± SD)[#]	6.83 ± 2.11
Total fentanyl high dose (>10 μg/day/kg) (mean ± SD)[#]	15.01 ± 4.31
Total fentanyl (μg/day) (mean ± SD)[#]	693.61 ± 341.79
Total fentanyl low dose (<500 μg/day) (mean ± SD)[#]	347.75 ± 102.24
Total fentanyl high dose (>500 μg/day) (mean ± SD)[#]	842.03 ± 298.39
Length of hospital stay (LOS) (mean ± SD)	14.57 ± 13.77

[§]*All analgesics were recalculated and recorded according to fentanyl equivalent dose as ratio of fentanyl:morphine = 100:1, fentanyl:alfentanyl = 10:1, fentanyl:pethidine = 1000:1.* [†]*NRSR 1st visit = numerical rating scale of pain at rest during 1st visit of patients, within 12 hours after return to ward.* [‡]*NRSM 1st visit = numerical rating scale of pain at movement during 1st visit of patients, within 12 hours after return to ward.* [#]*Total fentanyl = perioperative fentanyl dose + PCA-fentanyl dose. ASA: American Society of Anesthesiologists. BMI: Body mass index. PCA: Patient-controlled analgesia. SD: Standard deviation.*

TABLE 2. Factors influencing LOS of study population (Pearson correlation coefficient).

	LOS	
	Pearson correlation coefficient (PCC)	*p* value
	Preoperative factors	
Female	0.356	0.000*
BMI	−0.006	0.911
Age	0.220	0.000*
ASA classification	0.409	0.000*
Hemoglobin level	−0.167	0.001*
Diabetes mellitus	0.151	0.003*
Coronary artery disease	0.033	0.521
Hypertension	0.036	0.477
Cerebrovascular accident	0.016	0.760
Chronic kidney disease	−0.007	0.886
End-stage renal disease	0.035	0.493
	Perioperative factors	
Surgical time (min)	0.600	0.000*
Fentanyl (μg/kg)[§]	0.213	0.000*
Total intravenous fluid (mL/kg)	0.700	0.000*
Total intravenous fluid (mL/kg/hr)	0.268	0.000*
Blood transfusion	0.497	0.000*
Use of tetrastarch	−0.010	0.850
Tetrastarch (mL/kg)	−0.009	0.863
Total urine output (mL/kg/hr)	0.111	0.030*
Total urine output (mL/kg)	0.302	0.000*
Total blood loss (mL/kg)	0.518	0.000*

TABLE 2. Continuted.

	LOS	
	Pearson correlation coefficient (PCC)	*p* value
Postoperative factors		
NRSR at 1st visit[†]	−0.054	0.289
NRSM 1st visit[‡]	−0.059	0.249
Nausea during PCA	−0.075	0.142
Vomit during PCA	−0.045	0.384
Pruritus during PCA	0.165	0.001*
Abdomen distension during PCA	−0.017	0.740
PCA-fentanyl (μg/kg)	0.436	0.000*
PCA-fentanyl (μg/day/kg)	0.143	0.005*
PCA-fentanyl low dose (<10 μg/day/kg)	0.137	0.041*
PCA-fentanyl high dose (>10 μg/day/kg)	−0.05	0.531
PCA-fentanyl (μg/day)	0.174	0.001*
PCA-fentanyl low dose (<500 μg/day)	0.193	0.018*
PCA-fentanyl high dose (>500 μg/day)	0.074	0.260
Total fentanyl (μg/kg)[#]	0.440	0.000*
Total fentanyl (μg/day/kg)[#]	0.118	0.021*
Total fentanyl low dose (<10 μg/day/kg)[#]	0.073	0.328
Total fentanyl high dose (>10 μg/day/kg)[#]	−0.045	0.528
Total-fentanyl (μg/day)[#]	0.154	0.002*
Total fentanyl low dose (<500 μg/day)[#]	0.067	0.477
Total fentanyl high dose (>500 μg/day)[#]	0.056	0.357

[§]*All analgesics were recalculated and recorded according to fentanyl equivalent dose as ratio of fentanyl:morphine = 100:1, fentanyl:alfentanyl = 10:1, fentanyl:pethidine = 1000:1.* [†]*NRSR 1st visit = numerical rating scale of pain at rest during 1st visit of patients, within 12 hours after return to ward.* [‡]*NRSM 1st visit = numerical rating scale of pain at movement during 1st visit of patients, within 12 hours after return to ward.* [#]*Total fentanyl = perioperative fentanyl dose + PCA-fentanyl dose.* $*p < 0.05$. *ASA: American Society of Anesthesiologists. BMI: Body mass index. LOS: Length of hospital stay. PCA: Patient-controlled analgesia.*

TABLE 3. Factors influencing LOS in subgroup analysis (Pearson correlation coefficient).

	GS Laparotomy-Other disease (GLO) (n = 49)	GS Laparotomy-Liver- Transplant-Recipient (GLLTR) (n = 40)	GS Laparotomy-Liver-Transplant-Donor (GLLTD) (n = 44)	GS Laparotomy-Hepatectomy (GLH) (n = 89)	Gyn Laparotomy-Non- Cancer (GyLNC) (n = 103)	Gyn Laparotomy-Cancer (GyLC) (n = 58)
Preoperative factors						
ASA classification	−0.061	0.270	−0.074	0.221*	0.004	0.112
Hemoglobin level	−0.153	0.028	0.021	−0.013	0.065	−0.022
Diabetes mellitus	0.095	0.271	-	0.211*	0.093	0.096
Hypertension	−0.057	0.401*	-	0.150	0.279*	0.065
Chronic kidney disease	−0.122	-	-	−0.059	0.224*	0.326*
Female	0.108	−0.279	−0.022	0.146	−0.006	−0.089
Age	0.243	0.170	0.100	0.026	0.294*	0.236
Perioperative factors						
Surgical time (min)	0.093	0.139	0.293	0.352*	0.234*	0.657*
Fentanyl (μg/kg)[§]	−0.124	0.012	−0.034	0.034	0.064	−0.053
Total IV (mL/kg)	0.099	0.248	0.192	0.222*	0.409*	0.538*
Total IV (mL/kg/hr)	0.124	0.292	−0.337*	−0.027	0.135	0.117
Total urine (mL/kg)	0.154	0.146	0.097	0.103	0.182	0.159
Total urine (mL/kg/hr)	0.192	0.365*	−0.204	−0.038	0.064	−0.066
Total blood loss (mL/kg)	0.051	0.017	−0.019	0.375*	0.139	0.540*
Blood transfusion	0.035	0.141	−0.140	0.075	−0.057	0.757*
Use of tetrastarch	0.059	-	−0.015	0.260*	0.067	0.200
Tetrastarch (mL/kg)	0.057	-	−0.033	0.266*	0.098	0.346*
Postoperative factors						
Vomit during PCA	−0.106	-	−0.074	0.029	0.238*	−0.106
Pruritus during PCA	0.133	0.461*	0.219	−0.083	-	0.210
NRSM 1st visit[‡]	0.058	0.093	−0.107	0.015	−0.016	0.006
PCA-fentanyl (μg/kg)	0.007	0.112	−0.225	0.045	0.141	0.408*

TABLE 3. Continuted.

	GS Laparotomy-Other disease (GLO) (n = 49)	GS Laparotomy-Liver- Transplant-Recipient (GLLTR) (n = 40)	GS Laparotomy-Liver-Transplant-Donor (GLLTD) (n = 44)	GS Laparotomy-Hepatectomy (GLH) (n = 89)	Gyn Laparotomy-Non- Cancer (GyLNC) (n = 103)	Gyn Laparotomy-Cancer (GyLC) (n = 58)
PCA-fentanyl (μg/day)	−0.205	0.132	−0.330*	0.016	0.059	0.238
PCA-fentanyl low dose (<500 μg/day)	0.091	−0.195	0.197	0.184	0.039	0.049
PCA-fentanyl high dose (>500 μg/day)	0.150	0.148	−0.402*	0.028	0.198	0.096
PCA-fentanyl (μg/day/kg)	−0.158	0.207	−0.321*	−0.028	0.046	0.239
PCA-fentanyl low dose (<10 μg/day/kg)	−0.330	−0.064	−0.027	−0.118	0.080	0.125
PCA-fentanyl high dose (>10 μg/day/kg)	0.217	0.283	−0.397	−0.122	−0.007	0.124
Total fentanyl (μg)[#]	−0.132	0.057	−0.249	0.083	0.146	0.404*
Total fentanyl (μg/kg)[#]	0.002	0.112	−0.226	0.047	0.144	0.403*
Total fentanyl (μg/day/kg)[#]	−0.187	0.208	−0.326*	−0.027	0.032	0.177
Total fentanyl low dose (<10 μg/day/kg)[#]	−0.280	−0.352	−0.013	0.051	0.096	0.093
Total fentanyl high dose (>10 μg/day/kg)[#]	0.253	0.220	−0.437*	−0.049	0.121	0.013
Total fentanyl (μg/day)[#]	−0.232	0.128	−0.331*	0.023	0.050	0.171
Total fentanyl low dose (<500 μg/day)[#]	−0.003	−0.364	0.346	0.084	0.074	0.086
Total fentanyl high dose (>500 μg/day)[#]	0.002	0.163	−0.408*	−0.048	0.271*	0.261

[§]*All analgesics were recalculated and recorded according to fentanyl equivalent dose as ratio of fentanyl:morphine = 100:1, fentanyl:alfentanyl = 10:1, fentanyl:pethidine = 1000:1.* [‡]*NRSM 1st visit = numerical rating scale of pain at movement during 1st visit of patients, within 12 hours after return to ward.* [#]*Total fentanyl = perioperative fentanyl dose + PCA-fentanyl dose. *p < 0.05. ASA: American Society of Anesthesiologists. IV: Intraveous. LOS: Length of hospital stay. PCA: Patient-controlled analgesia.*

TABLE 4.1. Multiple linear regression analysis for GyLC group.

	Model (n = 58)		
	ß	SE	*p*-value
Chronic kidney disease	4.450	2.632	0.098
Surgery time (min)	1.682	3.517	0.635
Total IV (mL/kg)	0.054	0.066	0.420
Total blood loss (mL/kg)	−0.268	0.196	0.178
Blood transfusion (mL/kg)	7.824	2.205	0.001*
Tetrastarch (mL/kg)	0.087	0.192	0.652
PCA-fentanyl (μg/kg)	0.348	0.631	0.584
Total-fentanyl (μg)	−0.001	0.003	0.715
Total-fentanyl (μg/kg)	−0.229	0.653	0.727
Intercept	2.926	2.683	0.281

*Adjust R^2 = 0.579. *p < 0.05. ß: Beta coefficient. IV: Intraveous. GyLC: Gyn Laparotomy-Cancer. PCA: Patient-controlled analgesia. SE: Standard error.*

TABLE 4.2. Multiple linear regression analysis for GyLNC group.

	Model (n = 103)		
	ß	SE	*p*-value
Hypertension	2.240	1.530	0.146
Chronic kidney disease	12.693	5.335	0.019*
Age	0.090	0.062	0.151
Total IV (mL/kg)	0.152	0.055	0.007*
Surgery time (min)	−0.050	0.461	0.914
Vomit during PCA	5.670	2.195	0.011*
Intercept	−3.883	2.755	0.162

*Adjust R^2 = 0.263. *p < 0.05. ß: Beta coefficient. IV: Intraveous. GyLNC: Gyn Laparotomy-Non-Cancer. PCA: Patient-controlled analgesia. SE: Standard error.*

In the subgroup analysis, seven important opioid-related variables were found to have significant negative correlations with LOS in the GS laparotomy-liver transplant-donor (GLLTD) group. The straightforward interpretation of these interesting findings is that when higher cumulative dosages of opioids were used in the GS-laparotomy-liver transplant-donor (GLLTD) group, the LOS was shorter. Our institution has a living donor liver transplantation program with outstanding outcomes [24]. All healthy donor candidates are required to undergo strict preoperative examinations and preparation to ensure physical and psychological readiness for the surgical procedure. Appropriate postoperative pain control for these

TABLE 4.3. Multiple linear regression analysis for GLH group.

	Model (n = 89)		
	ß	SE	*p*-value
ASA classification	2.198	1.922	0.256
Surgery time (min)	0.803	1.885	0.671
Diabetes mellitus	3.311	2.212	0.138
Total IV (mL/kg)	−0.099	0.070	0.160
Total blood loss (mL/kg)	0.460	0.232	0.051
Tetrastarch infusion	−2.390	10.734	0.824
Tetrastarch (mL/kg)	0.547	1.422	0.701
Intercept	0.755	6.158	0.903

Adjust R^2 = 0.191. ASA: American Society of Anesthesiologists. ß: Beta coefficient. Intraveous. GLH: GS Laparotomy-Hepatectomy. SE: Standard error.

healthy individuals is important in terms of encouraging early ambulation as well as pulmonary hygiene, consequently reducing postoperative complications and shortening LOS [25].

After the subgroup analysis of multiple variables using PCC, a multiple linear regression analysis was carried out to assess the impact of the independent variables on LOS. It is found that blood transfusion was a critical independent factor that significantly predicted prolonged LOS in the GyLC group. This finding was similar to a report showing transfusion in non-cardiac patients was significantly associated with a slower and more eventful recovery [26]. Furthermore, although fentanyl-related variables had significant positive correlation with LOS based on the PCC analysis, these variables were insignificant in the multiple linear regression model. Therefore, fentanyl-related factors might not be able to predict prolonged LOS in GyLC patients using fentanyl-based IV PCA for postoperative pain control. Furthermore, chronic kidney disease, perioperative total intravenous fluid, and postoperative vomiting during PCA use were the three major factors that could be used clinically to predict increased LOS in the GyLNC group. Unfortunately, no factor was found to be valuable for LOS prediction in the GLH group.

There were limitations in this study. First, this was a retrospective observational study, so human medical record errors might happen. Thus, the quality of the clinical evidence is limited. Second, the study sample size was modest, which might have reduced the scope and complexity of some of the analyses. Third, the amount of opioids used by the patient after discontinuation of PCA was not analyzed, which might also affect LOS. Finally, the patients enrolled in this study were all Taiwanese; hence, the results might differ for other races or ethnicities. Therefore, a rigorous well-controlled randomized clinical study is needed in the future to verify our findings.

5. Conclusion

In conclusion, there are multiple factors that affect LOS in patients using PCA after laparotomy for different etiologies and surgical procedures. Acute pain physicians should take these factors into consideration when prescribing postoperative opioid-PCA dosages to minimize their impact on LOS.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

HCC, YHT and CKL—acquired and analyzed data. KHC and CHY—drafted, reviewed and edited the manuscript. All authors reviewed and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study protocol and the waiver of informed consent were approved by the institutional review boards (IRB number: 104–3603B) of Kaohsiung Chang Gung Memorial Hospital.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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