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Identification of predictors for acute postoperative pain after gynecological laparoscopy (STROBE-compliant article)

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Abstract

While the pain after gynecological laparoscopy is assumed to be minor, many women suffer from unexpected postoperative pain in the post-anesthesia care unit (PACU). Prior identification of these patients is significant for effective analgesia. Therefore, we sought to determine the predictors for acute postoperative pain after gynecological laparoscopy. The data of 280 patients undergoing gynecological laparoscopy were analyzed. Data included demographic characteristics, previous obstetric/gynecologic surgical history, menstruation pattern including dysmenorrhea severity, gynecological hormone administration history, and surgical data (surgical time, endometriosis severity, adhesion, drainage insertion, and surgery type). Univariate analysis and binary logistic regression were used to evaluate predictors for substantial pain in the PACU after gynecologic laparoscopy. Among the 280 patients, 115 (41%) suffered from substantial postoperative pain in the PACU. Whenever the level of dysmenorrhea became more severe (none → mild → moderate → severe), the risk of substantial pain in the PACU increased 2.9-fold (odds ratio [OR] 2.92, 95% confidence interval [CI] 2.11–4.03, $P < .001$). Moreover, patients undergoing laparoscopy for ectopic pregnancy had a higher risk of substantial pain compared with the others (OR 3.11, 95% CI 1.36–7.12, $P = .007$). Other factors did not show a significant association with substantial pain. Patients with preoperative severe dysmenorrhea and those undergoing laparoscopy for ectopic pregnancy should be considered to have a high risk of substantial postoperative pain in the PACU so that they receive prompt and aggressive analgesic intervention. In particular, dysmenorrhea severity is clinically valuable as a useful predictor for substantial pain after gynecological laparoscopy.

Abbreviations: BMI = body mass index, CI = confidence interval, IV PCA = intravenous patient-controlled analgesia, NRS = numerical rating scale, OR = odds ratio, PACU = post-anesthesia care unit, ROC = receiver operating characteristic curve, VIF = variance inflation factor.

Keywords: laparoscopy, postoperative pain, risk factor, women

1. Introduction

Gynecological laparoscopy is the most common surgery performed in women. Considering women are more sensitive to pain,[1] the expected decline in pain is a major advantage. However, many women patients suffer from unexpectedly substantial pain in the post-anesthesia care unit (PACU), leading to dissatisfaction with medical staffs or cardiopulmonary complications.[2] Therefore, it is significant to identify patients at high risk of postoperative pain for prompt and aggressive analgesic intervention in the early phase of recovery from anesthesia.

There have been many studies on predictors for postoperative pain, such as female gender, young age, preoperative pain, psychological factors, and surgical types.[1,3] However, even when these factors were homogeneously controlled, various levels of pain were observed in the PACU.[4] Therefore, more sophisticated preoperative exploration is required for these patients, who are sensitive to pain but still suffer from substantial postoperative pain.

Dysmenorrhea is a common symptom in these patients. However, there are substantial inter-individual differences in menstruation pain and women with severe dysmenorrhea have high level of prostaglandins.[5] This suggests that more severe preoperative dysmenorrhea may be associated with greater sensitivity to pain. While there may be an informative association between preoperative dysmenorrhea severity and pain intensity after gynecological laparoscopy, there has been no study about that. Therefore, we designed the present study to investigate this hypothesis. For a more complete predictive model, we included other gynecological factors in addition to dysmenorrhea severity.

2. Methods

The institutional review board of Catholic University approved the study and waived the requirement for obtaining informed consent due to the retrospective nature of this study.

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We reviewed the medical records of premenopausal women undergoing laparoscopy for gynecologic disease except cancer, at Seoul St. Mary's Hospital, Seoul, South Korea, between March 2016 and March 2018. For patients with predefined demographic and clinical characteristics, we performed data abstraction using the hospital's electronic charting system. The exclusion criteria were conversion to laparotomy during operation, pain disorders other than dysmenorrhea, psychiatric disorders, allergy to opioids, receiving any other concurrent surgical procedure during the operation, and pregnancy.

2.1. Routine clinical protocol (from preoperative area to PACU)

All patients scheduled to receive gynecological laparoscopy with general anesthesia at our hospital were routinely managed as follows: 1 day before surgery, all patients were taught to assess their pain using a numerical rating scale (NRS; 0=no pain and 10=the worst pain imaginable), and to use intravenous patient-controlled analgesia (IV PCA). No premedication, such as midazolam, was administered. In the operating room, propofol 1.5 to 2.5 mg/kg, remifentanil 0.5 to 1 ug/kg or fentanyl 0.5 to 1 ug/kg for induction, and rocuronium 0.6 to 0.8 mg/kg for tracheal intubation were administered. Anesthesia was maintained with remifentanil and sevoflurane in 40% to 50% air/oxygen to keep the bispectral index value between 30 and 60 and the baseline systolic blood pressure at +/−20%. Ventilation was controlled mechanically to maintain end-tidal CO_2 values of 30 to 40 mmHg. Additional rocuronium was administered as required. To prevent postoperative nausea and vomiting, all patients were given dexamethasone at induction and ramosetron at completion of surgery. The laparoscopy was performed under video guidance with three punctures in the abdomen. The intraperitoneal pressure was maintained around 12 mmHg. No local anesthetic was used during surgery. Remifentanil infusion was discontinued at the time of starting skin suturing. Ketorolac 30 mg and acetaminophen 1 g was intravenously injected for postoperative pain control. After confirmation of self-respiration, patients were extubated and transferred to the PACU.

Based on hospital protocol, if the patients complained of pain in the PACU, the anesthetic nurses were required to ask the patients to rate the pain severity using the NRS. If the pain was >4 on the NRS, fentanyl (0.5–1 ug/kg) was administered immediately. After 10 minutes of administration of fentanyl as a rescue analgesic, the anesthetic nurses asked each patient to provide an NRS pain severity score. If pain decreased below a score of 4, no further rescue analgesics were administered. If the patients continuously complained of pain after the first fentanyl administration, the nurses were required to notify the responsible anesthetist and then followed their additional orders. After the immediately acute pain was controlled, IV PCA (fentanyl 15 ug/kg in normal saline 100 mL, basal rate 1 mL/h, bolus 1 mL, lock-out time 10 minutes) was applied to all patients, and a loading dose was not administered.

2.2. Data collection

Because the data were obtained retrospectively, it was impossible to assess the postoperative pain intensity of all patients at the same time. Instead, we categorized patients requiring first rescue analgesic administration as those with substantial pain, because rescue analgesic was administered immediately when patients had an NRS pain rating >4; an abdominal pain rating >4 is generally regarded as moderate or severe.[6]

From patients' medical records, we obtained the following data: demographic characteristics [age and body mass index (BMI)], obstetric/gynecologic surgical history (open surgery including Caesarean section / non-open surgery such as hysteroscopy or laparoscopy), menstruation history (age at menarche, time since menarche, interval, amount, dysmenorrhea severity), abortion history (artificial/spontaneous), history of gynecological hormone administration including oral contraceptives or intrauterine device, and surgical data (surgical time, endometriosis severity, adhesions observed during laparoscopy, drainage insertion, surgery type).

2.3. Data analysis

To analyze the factors influencing the requirement for the first rescue analgesic, we used binary logistic regression. The requirement for the first rescue analgesic (yes or no) was an independent variable, and dependent variables were age, BMI, history of obstetric/gynecologic surgery (open/non-open), age at menarche, time since menarche, menstruation interval (regular/irregular), menstruation amount (scanty/mild/moderate/profuse), dysmenorrhea severity (none/mild/moderate/severe), abortion history (artificial/spontaneous), history of gynecological hormone administration, surgical time, endometriosis severity (none/stage I/stage II/stage III/stage IV) according to the American Society of Reproductive Medicine classification system,[7] adhesions, drainage insertion, and surgery type (laparoscopic hysterectomy/laparoscopic myomectomy/laparoscopic ectopic pregnancy surgery/laparoscopic cystectomy/other laparoscopy). We used the variance inflation factor (VIF) to identify multicollinearity between independent variables and then analyzed independent variables without multicollinearity (VIF < 10).

For univariate analysis, we used the Chi-square test (categorical data), Armitage trend test (dysmenorrhea severity, menstruation amount, endometriosis severity), or Student's t test (continuous data). All variables that were significant at $P < .1$ were analyzed in binary logistic regression (stepwise method). For the goodness-of-fit test of the multivariate model, we performed the Hosmer & Lemeshow test. The predictive utility of these factors was further evaluated by the area under the receiver operating characteristic curve (ROC area). The P values < .05 were considered statistically significant. The statistical analysis was done using SPSS for Windows software (ver. 18.0; SPSS Inc., Chicago, IL).

3. Results

A total of 359 patients underwent laparoscopy for gynecologic disease except cancer during the study period. The data for 280 patients with inclusion criteria were analyzed (Fig. 1). Among the 280 patients, 115 (41%) required a rescue analgesic due to pain (NRS > 4) in the PACU. As mentioned above, we categorized those patients as having substantial pain. There were no significant differences in demographic data between the substantial pain group and the other group (Table 1).

Obstetric/gynecologic history, except dysmenorrhea severity, had no significant association with pain in the PACU. Similarly, endometriosis severity, adhesion, drain insertion, and intraoperative remifentanil dosage were not associated with substantial postoperative pain. On the other hand, surgery time was
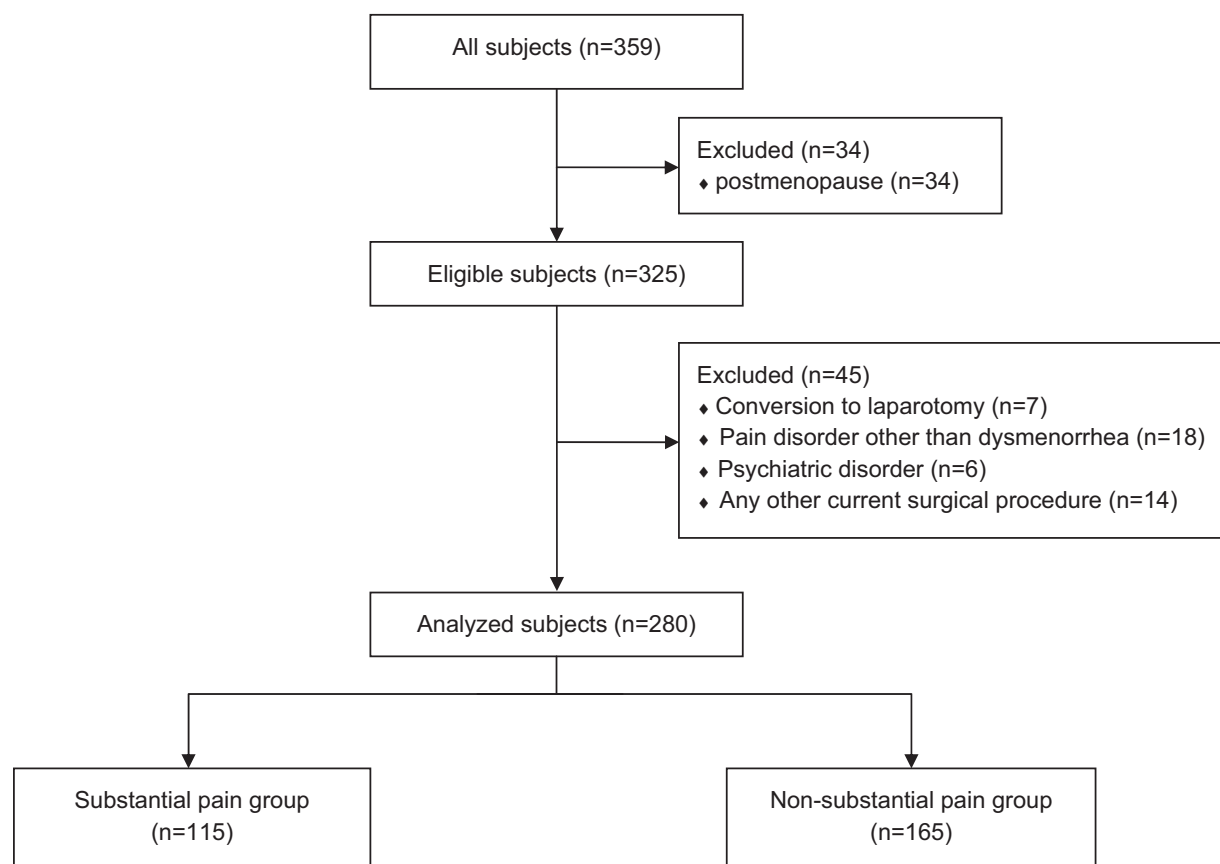
Figure 1. Diagram showing the flow of participants.

significantly associated with postoperative pain. The duration of surgery in patients with substantial postoperative pain was 16 minutes longer than that in the other patient group ($P = .014$, Table 1).

A history of non-open obstetric/gynecologic surgery had a significant association with substantial postoperative pain. In total, 64% (18/28) of patients with a history of non-open obstetric/gynecologic surgery developed substantial pain in the PACU ($P = .008$), whereas 36% (24/67) of patients with a history of open obstetric/gynecologic surgery developed substantial pain ($P = .317$).

The severity of preoperative dysmenorrhea was significantly associated with postoperative pain in the PACU. Among all patients, 80% (224/280) had preoperative dysmenorrhea, and among them, 46% (103/224) had more than moderate dysmenorrhea. According to the Armitage trend analysis, the more severe the preoperative dysmenorrhea, the more frequent was the substantial pain in the PACU ($P < .001$, Fig. 2). Only 18% of patients without any preoperative dysmenorrhea had substantial pain in the PACU, whereas 86% of patients with severe preoperative dysmenorrhea had substantial pain.

Table 2 shows the types of laparoscopy. In total, 63% of patients receiving laparoscopy for ectopic pregnancy had substantial pain in the PACU ($P = .003$), whereas the other surgical types were not associated with substantial postoperative pain. Sixty patients received 2 types of surgery simultaneously. Among them, 33 underwent myomectomy and cystectomy and 27 underwent hysterectomy and cystectomy. No significant

association was observed between the number of surgeries and prevalence of substantial pain ($P = .225$).

On univariate analysis, independent variables significantly associated with substantial pain at $P < .1$ were a history of non-open obstetric/gynecologic surgery, dysmenorrhea severity, surgical time, and laparoscopic ectopic pregnancy surgery (Table 3). There was no multicollinearity among the dependent variables.

In the multiple logistic regression analysis, dysmenorrhea severity and laparoscopic ectopic pregnancy remained significantly associated with substantial pain. The risk of substantial pain increased 2.9-fold [odds ratio (OR) 2.92, 95% confidence interval (CI) 2.11–4.03, $P < .001$] for each increase in dysmenorrhea severity category (i.e., severe vs moderate, moderate vs mild, mild vs none). Moreover, patients receiving laparoscopic ectopic pregnancy surgery had a higher risk of substantial pain compared with the other patients (OR 3.11, 95% CI 1.36–7.12, $P = .007$). The constant remained significant, and the reliability of this model was good (the P value of the Hosmer and Lemeshow test was .477). This multivariate model yielded a ROC area of 0.77 (95% CI 0.71~0.83, $P < .001$).

4. Discussion

In this study, 41% of patients undergoing gynecological laparoscopy suffered from substantial pain in the PACU. The severity of dysmenorrhea (none/mild/moderate/severe) was a predictor for substantial pain. For example, patients with severe

Table 1

Demographic, preoperative, and operative data of patients with and without substantial pain in the post-anesthesia care unit.

	Substantial pain (n = 115)	Non-Substantial pain (n = 165)	P value
Demographic data			
Age, yr	39 ± 1	39 ± 2	.564
BMI, kg/m²	22.5 ± 3.0	22.5 ± 3.3	.959
ASA physical status I/II	57/58	80/85	.892
Obstetric/gynecologic history			
Age at menarche, years	14 ± 1	14 ± 2	.482
Time since menarche, years	25 ± 8	26 ± 9	.634
Interval of menstruation			.890
Regular	101 (88%)	144 (87%)	
Irregular	14 (12%)	21 (13%)	
Amount of menstruation			.856
Scanty	8 (7%)	13 (8%)	
Mild	17 (15%)	28 (17%)	
Moderate	59 (51%)	76 (46%)	
Profuse	31 (27%)	48 (29%)	
Spontaneous abortion history	13 (11%)	19 (12%)	.957
Artificial abortion history	36 (31%)	52 (32%)	.970
Hormone medication history	5 (4%)	14 (8%)	.176
Surgical and anesthetic data			
Severity of endometriosis			.437
None	78 (68%)	122 (74%)	
Stage I	7 (6%)	12 (7%)	
Stage II	6 (5%)	6 (4%)	
Stage III	7 (6%)	11 (7%)	
Stage IV	17 (15%)	14 (8%)	
Adhesion confirmed by laparoscopy	54 (47%)	72 (43%)	.583
Drainage tube insertion	43 (37%)	62 (38%)	.975
Remifentanil dosage; ug	104.7 ± 36.2	97.2 ± 31.3	.471
Surgical time; min	123.8 ± 55.4	107.6 ± 53.6	.014

Values are as means ± SD or number (%).
ASA = American Society of Anesthesiologists, BMI = body mass index.

dysmenorrhea had a 2.9-fold higher risk than those with moderate dysmenorrhea. Laparoscopic ectopic pregnancy surgery was associated with a 3.1-fold higher risk compared to other types of laparoscopy.

Generally, pain after laparoscopy is assumed to be minor. Therefore, patients and surgeons expect the pain after laparoscopy to be mild, such that specific treatment will not be necessary. However, unexpected results have aroused suspicion regarding that assumption, which was confirmed by our results showing that 41% of patients required a rescue analgesic in the PACU.

This is supported by a large prospective study with 179 types of surgery.[4] The authors reported that minor-to-medium-level surgical procedures (including laparoscopy) caused unexpectedly high levels of postoperative pain and 70% of patients did not receive adequate analgesia. This was caused by medical staff misjudgement that the pain after minor surgery would be minor. Considering that the patients undergoing gynecological laparoscopy are women, who are more sensitive to pain,[3] it is more important to identify the women patients with substantial predictors for postoperative pain.

The known predictors of postoperative pain are gender, preoperative pain, anxiety, age, surgical type, and incision size (>10 cm).[1,3] While our study used a retrospective analysis, we limited our subjects to patients who were premenopausal (i.e., not elderly) women, scheduled for gynecologic laparoscopy, and had

no psychiatric disease. Therefore, it was possible to control some predictors (i.e., age, gender, surgical type, incision size, psychiatric disorder) except preoperative pain severity.

Preoperative pain sensitivity is known as a strong predictor for postoperative pain. It can be measured using various methods, such as pressure, heat, cold, electrical pain sensitivity, or a pain questionnaire.[8–12] However, these measurement methods require some degree of time and effort from medical staff. Therefore, they seem inconvenient in clinical practice. On the contrary, information on the severity of dysmenorrhea can be obtained more easily based on medical records or a simple question. Therefore, this is a useful method to identify patients at high risk of postoperative pain, instead of experimental pain sensitivity.

While dysmenorrhea is a common symptom in women,[13] there are substantial inter-individual differences in pain, as showed in our results. These differences may be explained by the prostaglandin theory: during menstruation, the endometrial cells release prostaglandins, leading to pain.[5] Interestingly, women with more severe dysmenorrhea have higher levels of prostaglandins.[13] This suggests that more severe preoperative dysmenorrhea may be associated with greater sensitivity to pain. This suggestion is consistent with several previous reports. First, prostaglandin causes the sensitization of peripheral nociceptors, leading to a hyperplastic state of the spinal cord.[14] Second, Vincent et al[15] reported a higher incidence of suppression of the hypothalamus–pituitary–adrenal axis and reduced quality of life in the dysmenorrhea group, all of which are well-known features of chronic pain conditions. These suggest that the severity of dysmenorrhea could be used as an important predictor of postoperative pain after gynecological laparoscopy.

Although we intentionally controlled for the type of surgery (gynecological laparoscopy), our result revealed that laparoscopic ectopic pregnancy surgery caused more substantial pain compared with other laparoscopies. Our findings correspond to the results of a large prospective study showing that laparoscopic ectopic pregnancy surgery was the most painful among all the gynecological laparoscopies.[4] While the mechanism is unclear, these can be based on the emergent nature of this surgery. In the systematic review, emergency surgery was reported to be a strong predictor for postoperative analgesic consumption.[3] There may be less preoperative information available for patients who have undergone emergency operations, as well as less time for psychological preparation, resulting in an increased requirement for postoperative analgesia.

Our results showed that the severity of endometriosis did not have a significant effect on postoperative pain. In accordance with our result, the severity of endometriosis is known to be discordant with the severity of dysmenorrhea.[16] It is highly plausible that dysmenorrhea is composed of complex factors, including emotional and behavioral components, as well as the simple pathophysiologic factors observed in endometriosis.

Recent developments in anesthetic techniques have led to rapid awakening after surgery. The use of short-acting drugs (e.g., remifentanil) allows prompt recovery, which is inevitably accompanied by rapid perception of postoperative pain in the PACU. Therefore, identification of the patients with greater pain sensitivity would be required for preemptive or early intervention for acute pain, minimizing side effects. In this clinical setting, preoperative evaluation of dysmenorrhea severity is thought to be a simple and informative method.
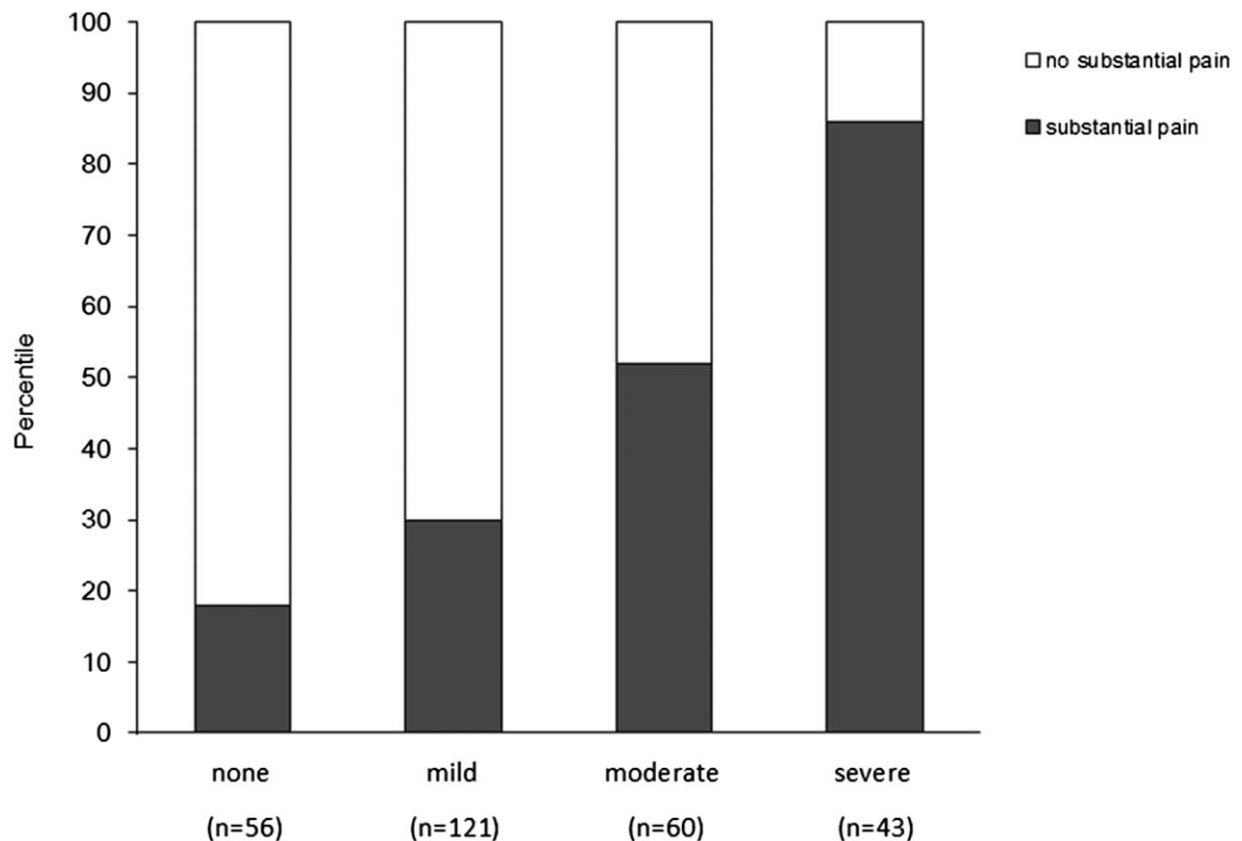
Figure 2. The distribution of substantial postoperative pain in the post-anesthesia care unit according to the severity of preoperative dysmenorrhea. Values are percentile. $P < .001$ among 4 groups.

The present study had some limitations. First, it used data from a single academic medical center. However, the anesthetic care and acute pain treatment provided in our hospital correspond with common clinical practice. Second, due to the retrospective nature of this study, we could not assess the pain level at predefined time points. However, because patients with pain ratings >4 on the NRS were given rescue analgesic in the PACU, and we included those patients in the substantial pain group, we believe it is possible to appropriately identify patients with acute postoperative pain. Third, because of the retrospective nature of this study, we might not have completely excluded the patient with preoperative anxiety, which is regarded as a powerful

predictor of postoperative pain. Further prospective studies including these factors such as preoperative anxiety or genetic trait are required for the more complete predictive model for postoperative pain.

In conclusion, our study demonstrates that preoperative dysmenorrhea severity and ectopic pregnancy laparoscopic surgery are strong predictors of postoperative pain after gynecological laparoscopy in the PACU. Especially, preoperative dysmenorrhea severity is clinically valuable as a simple and useful predictor. We believe our data provides better insight into predictors, which future prospective studies on the postoperative pain of women should take into consideration.

Table 2

The distribution of substantial postoperative pain in the post-anesthesia care unit according to the type of laparoscopy.

	Substantial pain	Non-substantial pain	P value
Lap. hysterectomy (n=115)	49 (43%)	66 (57%)	.662
Lap. myomectomy (n=67)	27 (41%)	40 (59%)	.883
Lap. ectopic pregnancy surgery (n=38)	24 (63%)	14 (37%)	.003
Lap. cystectomy (n=147)	63 (43%)	84 (57%)	.523
Diagnostic laparoscopy (n=10)	5 (50%)	5 (50%)	1.000

Values are as number (%). Lap=laparoscopic.

Table 3

Binary logistic regression to evaluate the effect of specific variables on the probability of substantial pain in the post-anesthesia care unit.

	OR	95% CI	P value
Dysmenorrhea severity (none/mild/moderate/severe)	2.92	2.11–4.03	<.001
Non-open OBGY surgical history (Yes)	1.45	0.58–3.64	.429
Lap. ectopic pregnancy surgery (Yes)	3.11	1.36–7.12	.007
Surgical time (unit: min)	1.01	1.00–1.01	.069

Nagelkerke's $R^2 = .300$, Hosmer & Lemeshow's $x^2 = 7.568$, $P = .477$.
CI=confidence interval, Lap=laparoscopic, OBGY=obstetric/gynecologic, OR=odds ratio.

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Author contributions

Jin Joo performed data analysis and wrote the first draft of this paper. Hyun Kyung Moon did statistical design, data collection and data analysis. Young Eun Moon performed study design, data analysis and revising the draft.

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