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ORIGINAL RESEARCH

Risk factors of different types of acute pain after laparoscope-assisted vaginal hysterectomy

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Abstract

Purpose: Previous study has shown that acute pain after laparoscope-assisted vaginal hysterectomy (LAVH), which consists of several pain components, like somatic pain, visceral pain, shoulder pain, and low back pain (LBP). Potential risk factors of postoperative pain remain unclear. This study aimed to determine risk factors for different types of acute postoperative pain and provide guidance for personalized analgesic medication programs.

Patients and methods: This was a prospective, observational cohort study, in which 287 patients undergoing LAVH between January, 2017 and September, 2018 at the First Affiliated Hospital of Wenzhou Medical University, China were included. Univariate and multivariable logistic regression analyses were used to evaluate risk factors for the different types of acute pain after LAVH.

Results: In the total cohort, visceral pain and LBP were the most common complaints of patients, followed by somatic pain and shoulder pain. Multivariable analysis revealed that postoperative nausea and vomiting, BMI and main indication for surgery were associated with acute postoperative visceral pain. Preoperative chronic pain, BMI, preoperative anxiety and the number of trocars were associated with acute postoperative LBP, while occupation, pelvic adhesions, and history of abdominal surgery were risk factors for acute postoperative somatic pain.

Conclusion: Our study highlights that acute postoperative visceral pain and LBP are main components of pain after LAVH, and different types of acute pain after LAVH are correlated with preoperative, intraoperative and postoperative factors. Acute postoperative pain has unique risk factors according to the component type.

Keywords

Risk factors; Visceral pain; Low back pain; Somatic pain; Laparoscope-assisted vaginal hysterectomy

1. Introduction

According to a US national survey, 86% of patients experienced pain after surgery, and a high proportion of 75% of those patients experienced moderate to severe pain during the immediate postsurgical period [1]. Although local anesthetics, opiates, or cyclo-oxygenase (COX) inhibitors that are administered intraoperatively and immediately after operation achieve successful pain control, acute postoperative pain remains a major clinical problem and the most frequent complaint of patients. Pain sensitivity varies according to individual difference, and pain ratings of identical noxious stimuli may span the entire visual analogue scale (VAS) [2, 3]; moreover, acute postoperative pain attained high prevalence in Chinese patients undergoing surgery.

Compared with abdominal hysterectomy, laparoscopic hysterectomy has many advantages, such as small abdominal incision, fewer complications, shorter hospital stay, faster recovery of normal life and work, and good acceptance by patients [4, 5]. Laparoscopic surgery was introduced as a minimally invasive operation, but studies showed that it may be associated with severe pain and strong need for analgesia immediately after surgery [6]. The average of postoperative pain after hysterectomy under general anesthesia was approximately 3-6 on numerical rating scale (NRS) ranging from 0 to 10 [7–9], and clinicians should consider this fact during case management.

Despite increasing understanding of acute postoperative pain in terms of mechanisms, treatment options, and evidence-based management guidelines [10], the predictors of pain in routine clinical practice remain unclear. Reports indicated several risk factors for acute postoperative pain such as preoperative pain, type of surgery, age, body mass index (BMI), and psychosocial factors [11–14], but to the best of our knowledge, no study has focused on risk factors for different types of acute postoperative pain after laparoscope-assisted

TABLE 1. Demographic and patient characteristics on baseline before surgery for laparoscope-assisted vaginal hysterectomy

Variables	Complete cohort	Excluded or lost	*P* value
	n = 287	n = 120	
Age (year), Mean ± SD	49.20 ± 6.79	49.64 ± 6.54	0.54
Medical Insurance Type, n (%)			0.47
No	23 (8)	10 (8.33)	
New Type Of Rural Cooperative	195 (67.9)	73 (60.83)	
Urban Residents	10 (3.5)	7 (5.83)	
Urban Workers	59 (20.6)	30 (25)	
Education, n (%)			0.53
Illiteracy	71 (24.7)	35 (29.2)	
Primary School	123 (42.9)	42 (35)	
Middle And High School	75 (26.1)	35 (29.17)	
College And Higher	18 (6.3)	8 (6.67)	
Occupation, n (%)			0.06
No	170 (59.2)	59 (49.2)	
Yes	117 (40.8)	61 (50.8)	
Hypertension, n (%)			0.64
No	226 (78.7)	97 (80.8)	
Yes	61 (21.3)	23 (19.2)	
Diabetes, n (%)			0.28
No	270 (94.1)	116 (96.7)	
Yes	17 (5.9)	4 (3.3)	
A History Of Abdominal Surgery, n (%)			0.17
No	213 (74.2)	81 (67.5)	
Yes	74 (25.8)	74 (32.5)	
Cesarean Section, n (%)			0.12
No	253 (88.2)	112 (93.3)	
Yes	34 (11.8)	8 (6.7)	
Dysmenorrhea, n (%)			0.08
No	187 (65.2)	187 (74.2)	
Yes	100 (34.8)	31 (25.8)	
BMI (kg/m^2) , Mean ± SD	23.67 ± 2.96	23.60 ± 2.37	0.85
Main indication for surgery, n (%)			0.10
Physical Findings	179 (62.4)	60 (50)	
Descensus Uteri	15 (5.2)	6 (5)	
Changes In Menstruation	68 (23.7)	42 (35)	
Dysmenorrhea	25 (8.7)	12 (10)	
Preoperative Chronic Pain, n (%)			0.13
No	201 (70)	93 (77.5)	
Yes	86 (30)	27 (22.5)	
Exercise Habit, n (%)			0.80
No	219 (76.3)	93 (77.5)	
Yes	68 (23.7)	27 (22.5)	
The Level Of Anxiety, n (%)			0.14
Mild	213 (74.2)	99 (82.5)	
Moderate	44 (15.3)	10 (8.3)	
Severe	30 (10.5)	11 (9.2)	

Data are presented as n (%) or mean ± standard deviation.
Statistics are t test, sank sum test or chi-square test wherever appropriate.

vaginal hysterectomy (LAVH).

Based on these facts, we performed the present prospective, observational cohort study to support that acute pain after LAVH consists of several pain components: somatic pain, visceral pain, shoulder pain and low back pain (LBP) [15, 16]; the hypothesis of the study is that there are differences in risk factors of acute pain according to symptom location.

2. Methods

TABLE 2. Incidence of different types of postoperative pain

Type of pain	NO, n (%)	Mild, n (%)	Moderate, n (%)	Severe, n (%)
Visceral pain	33 (11.50)	129 (44.95)	69 (24.04)	56 (19.51)
Somatic pain	83 (28.92)	140 (48.78)	58 (20.21)	6 (2.10)
Low back pain	67 (23.34)	112 (39.02)	63 (21.95)	45 (15.68)
Shoulder pain	243 (84.67)	28 (9.76)	9 (3.14)	7 (2.44)

Values are presented as n (%).

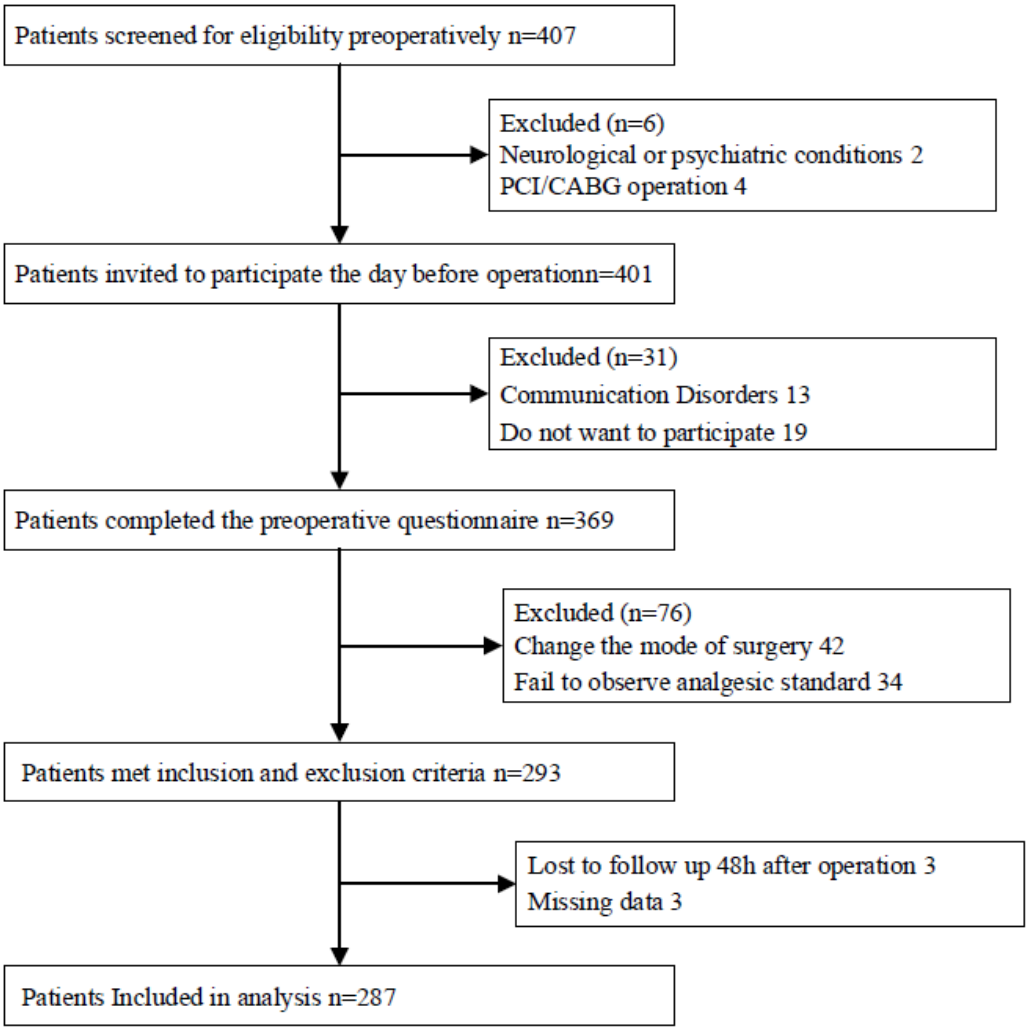

FIGURE 1. Flowchart of the patients.

2.1 Study design and participant recruitment

This prospective, observational cohort study was approved by the Ethics Committee (2019-030) in Clinical Research of the First Affiliated Hospital of Wenzhou Medical University and was registered at China Clinical Trial Registry: ChiCTR-ROC-17013036. Patients scheduled for LAVH at the Gynecology Department at First Affiliated Hospital of Wenzhou Medical University between January, 2017 and October, 2018 were enrolled in the study on the day before surgery. Written informed consent was obtained from every participant by preoperative interview on the same day; subsequently, data of patient characteristics were collected. Data of futher information about the surgery, anesthesia and pain were collected by researcher on the day of operation and 24 h, 48 h after operation. Data of all patients who completed the entire study were submitted to analysis.

From January, 2017 to October, 2018, indices of potential acute postoperative pain were recorded in a single database. Patients scheduled for LAVH under general anesthesia were recruited; at the time of registration, eligible patients were $>$ 18 years-old. Those with serious psychological disorder and other significant cardiovascular, respiratory, hepatic and

TABLE 3. Univariate analysis of risk factors of acute postoperative visceral pain

	No Pain Or Mild Pain, n (%)	Moderate To Severe Pain, n (%)	*P* value	OR (95% CI)
Preoperative variable				
Age			0.36	
≤ 45	42 (25.9)	38 (30.4)		
45-55	93 (57.4)	73 (58.4)	0.60	0.87 (0.51-1.48)
> 55	27 (16.7)	14 (11.2)	0.16	0.57 (0.26-1.25)
Medical Insurance Type			0.20	
No	14 (8.6)	9 (7.2)		
New Type Of Rural Cooperative	112 (69.1)	83 (66.4)	0.75	1.15 (0.48-2.79)
Urban Residents	8 (4.9)	2 (1.6)	0.29	0.39 (0.07-2.26)
Urban Workers	28 (17.3)	31 (24.8)	0.28	1.72 (0.65-4.59)
Education			0.22	
Illiteracy	41 (25.3)	30 (24)		
Primary School	73 (45.1)	50 (40)	0.83	0.94 (0.52-1.69)
Middle And High School	42 (25.9)	33 (26.4)	0.83	1.07 (0.56-2.07)
College And Higher	6 (3.7)	12 (9.6)	0.07	2.73 (0.92-8.11)
Occupation			0.46	
No	99 (61.1)	71 (56.8)		
Yes	63 (38.9)	54 (43.2)	0.46	1.2 (0.74-1.92)
Hypertension			0.10	
No	122 (75.3)	104 (83.2)		
Yes	40 (24.7)	21 (16.8)	0.11	0.62 (0.34-1.11)
Diabetes			0.08	
No	149 (92)	121 (96.8)		
Yes	13 (8)	4 (3.2)	0.10	0.38 (0.12-1.19)
A History Of Abdominal Surgery			0.54	
No	118 (72.8)	95 (76)		
Yes	44 (27.2)	30 (24)	0.54	0.85 (0.5-1.45)
Cesarean Section			0.42	
No	145 (89.5)	108 (86.4)		
Yes	17 (10.5)	17 (13.6)	0.42	1.34 (0.66-2.75)
Parity			0.90	
≤ One	53 (32.7)	40 (32)		
Two	75 (46.3)	61 (48.8)	0.78	1.08 (0.63-1.83)
> Two	34 (21)	24 (19.2)	0.84	0.94 (0.48-1.82)
Abortion			0.42	
≤ One	62 (38.3)	49 (39.2)		
Two	44 (27.2)	41 (32.8)	0.57	1.18 (0.67-2.08)
> Two	56 (34.6)	35 (28)	0.42	0.79 (0.45-1.39)
Dysmenorrhea			0.27	
No	110 (54.6)	77 (61.6)		
Yes	52 (45.4)	48 (38.4)	0.27	1.32 (0.81-2.15)
BMI			0.03	
< 24	82 (67.9)	79 (63.2)		
≥ 24	80 (32.1)	46 (36.8)	0.03	0.6 (0.37-0.96)
Main indication for surgery			0.01	
Physical Findings	98 (60.5)	81 (64.8)		
Descensus Uteri	14 (8.6)	1 (0.8)	0.02	0.09 (0.01-0.67)
Changes In Menstruation	34 (21)	34 (27.2)	0.50	1.21 (0.69-2.12)
Dysmenorrhea	16 (9.9)	9 (7.2)	0.39	0.68 (0.29-1.62)
Preoperative Chronic Pain			0.51	
No	116 (71.6)	85 (68)		
Yes	46 (28.4)	40 (32)	0.51	1.18 (0.71-1.97)
Exercise Habit			0.70	
No	125 (77.2)	94 (75.2)		
Yes	37 (22.8)	31 (24.8)	0.70	1.11 (0.64-1.93)
The Level Of Anxiety			0.63	
Mild	117 (72.2)	96 (76.8)		
Moderate	26 (16)	18 (14.4)	0.61	0.84 (0.44-1.63)
Severe	19 (11.7)	11 (8.8)	0.39	0.71 (0.32-1.55)

TABLE 3. Continued

	No Pain Or Mild Pain, n (%)	Moderate To Severe Pain, n (%)	*P* value	OR (95% CI)
Pelvic Adhesions			0.39	
No	101 (62.4)	84 (67.2)		
Yes	61 (37.6)	41 (32.8)	0.39	0.81 (0.5-1.32)
The Number Of Trocar			0.74	
Three	72 (44.4)	58 (46.4)		
≥ Four	90 (55.6)	67 (53.6)	0.74	0.92 (0.58-1.48)
Uterine Size			0.29	
Atrophy	20 (12.3)	15 (12)		
Normal	19 (11.7)	7 (5.6)	0.20	0.49 (0.16-1.47)
First Trimester Of Pregnancy	55 (34)	50 (40)	0.63	1.21 (0.56-2.62)
Second Trimester Of Pregnancy	68 (42)	53 (42.4)	0.92	1.04 (0.49-2.22)
Bleeding volume			0.7	
≤ 20	88 (54.3)	65 (52)		
20-50	49 (30.2)	36 (28.8)	0.98	0.99 (0.58-1.7)
> 50	25 (15.4)	24 (19.2)	0.43	1.3 (0.68-2.48)
Operative time			0.5	
≤ 120min	131 (80.9)	97 (77.6)		
> 120 min	90 (19.1)	28 (22.4)	0.50	1.22 (0.69-2.17)
Post-Operative Nausea And Vomiting			0.04	
No	120 (74.1)	75 (60)		
Only Nausea	12 (7.4)	16 (12.8)	0.06	2.13 (0.96-4.76)
Vomiting	30 (18.5)	34 (27.2)	0.04	1.81 (1.03-3.2)
Time Of Pelvic Drainage			0.78	
One Day	128 (79)	96 (76.8)		
Two Days	25 (15.4)	23 (18.4)	0.52	1.23 (0.66-2.29)
Three Days Or More	9 (5.6)	6 (4.8)	0.83	0.89 (0.31-2.58)
The Indwelling Catheter Time			0.35	
No or One Day	22 (13.6)	24 (18.5)		
Two Days	67 (41.4)	47 (37.6)	0.21	0.64 (0.32-1.28)
Three Days Or More	73 (45.1)	54 (43.2)	0.26	0.67 (0.34-1.33)
Volume of pelvic drainage in 24 h			0.51	
≤ 50	57 (35.2)	48 (38.4)		
50-100	53 (32.7)	33 (26.4)	0.31	0.74 (0.41-1.32)
> 100	52 (32.1)	44 (35.2)	0.99	1 (0.58-1.75)

Values are presented as n (%);
OR, odds ratio; CI, Confidence interval;
Binary logistic regression analysis.

kidney diseases were excluded; other exclusion criteria were limitations of self-expression or language problems, pregnant mothers, and nursing mothers.

2.2 Types of outcomes

For development of risk assessment models, the primary outcome was incidence and intensity of acute postoperative pain, including somatic pain, visceral pain, shoulder pain, and LBP. Intra-abdominal pain (visceral pain) was defined as pain within the abdomen, which may be deep, dull, and more difficult to localize, but that may be predominantly located in the hypogastrium. Somatic pain was a superficial pain localized in the wounds that were sensitive to touch. Shoulder pain was defined as pain sensation in the shoulder(s) [9, 17]. Low back pain (LBP) was defined as pain located between the 12th rib and the inferior gluteal folds, with or without leg pain according to a previous study [18].

Pain intensity was assessed using NRS from 0 to 10, with zero representing no pain and 10 representing worst imaginable pain [19], and categorized into two groups: no pain or mild pain, 0 to 3; moderate to severe pain, 4 to 10 [8, 20].

The secondary outcomes were (1) postoperative complications, such as respiratory depression, bleeding, and fever and (2) length of hospital stay, exhaust time, and time to get out of bed.

2.3 Data collection

Data collection and processing were completed by three anesthesiologists and four college students; preoperative data were collected and checked by two college students and entered by two other college students all who completed 1 week's training for their respective tasks. Two anesthesiologists were responsible for intraoperative anesthesia and administration of analgesia, and two university students, for intraoperative data collection. Follow-up was conducted by another anesthesiologist who was blinded to preoperative and intraoperative data, which included pain assessment, and management of postoperative pain and other complications.

TABLE 4. Univariate analysis of risk factors of acute postoperative low back pain

	No Pain Or Mild Pain N (%)	Moderate To Severe Pain N (%)	*P* value	OR (95% CI)
Preoperative variable				
Age			0.11	
≤ 45	57 (31.8)	23 (21.3)		
45-55	100 (55.9)	66 (61.1)	0.09	1.64 (0.92-2.91)
> 55	22 (12.3)	19 (17.6)	0.06	2.14 (0.98-4.68)
Medical Insurance Type			0.18	
No	19 (10.6)	4 (3.7)		
New Type Of Rural Cooperative	119 (66.5)	76 (70.4)	0.05	3.03 (0.99-9.26)
Urban Residents	6 (3.4)	4 (3.7)	0.17	3.17 (0.6-16.69)
Urban Workers	35 (19.6)	24 (22.2)	0.05	3.26 (0.98-10.78)
Education			0.75	
Illiteracy	45 (25.1)	26 (24.1)		
Primary School	74 (41.3)	49 (45.4)	0.66	1.15 (0.63-2.09)
Middle And High School	50 (27.9)	25 (23.1)	0.68	0.87 (0.44-1.71)
College And Higher	10 (5.6)	8 (7.4)	0.54	1.38 (0.49-3.95)
Occupation			0.33	
No	110 (61.5)	60 (55.6)		
Yes	69 (38.5)	48 (44.4)	0.33	1.28 (0.79-2.07)
Hypertension			0.76	
No	142 (79.3)	84 (77.8)		
Yes	37 (20.7)	24 (22.2)	0.76	1.1 (0.61-1.96)
Diabetes			0.41	
No	170 (95)	100 (92.6)		
Yes	9 (5)	8 (7.4)	0.41	1.51 (0.56-4.04)
A History Of Abdominal Surgery			0.17	
No	128 (71.5)	85 (78.7)		
Yes	51 (28.5)	23 (21.3)	0.18	0.68 (0.39-1.19)
Cesarean Section			0.06	
No	153 (85.5)	100 (92.6)		
Yes	26 (14.5)	8 (7.4)	0.08	0.47 (0.2-1.08)
Parity			0.93	
≤ One	58 (32.4)	35 (32.4)		
Two	86 (48)	50 (46.3)	0.89	0.96 (0.56-1.66)
> Two	35 (19.6)	23 (21.3)	0.8	1.09 (0.56-2.13)
Abortion			0.56	
≤ One	67 (37.4)	44 (40.7)		
Two	57 (31.8)	28 (25.9)	0.34	0.75 (0.41-1.35)
> Two	55 (30.7)	36 (33.3)	0.99	1 (0.57-1.76)
Dysmenorrhea			0.55	
No	119 (66.5)	68 (63.0)		
Yes	60 (33.5)	40 (37.0)	0.55	1.17 (0.71-1.92)
BMI			0.04	
< 24	92 (51.4)	69 (63.9)		
≥ 24	87 (48.6)	39 (36.1)	0.04	0.6 (0.37-0.98)
Main indication for surgery			0.06	
Physical Findings	107 (59.8)	72 (66.7)		
Descensus Uteri	7 (3.9)	8 (7.4)	0.33	1.7 (0.59-4.89)
Changes In Menstruation	51 (28.5)	17 (15.7)	0.03	0.5 (0.27-0.93)
Dysmenorrhea	14 (7.8)	11 (10.2)	0.72	1.17 (0.5-2.72)
Preoperative Chronic Pain				< 0.01
No	143 (79.9)	58 (53.7)		
Yes	36 (20.1)	50 (46.3)	< 0.01	3.42 (2.02-5.79)
Exercise Habit			0.91	
No	137 (76.5)	82 (75.9)		
Yes	42 (23.5)	26 (24.1)	0.91	1.03 (0.59-1.81)
The Level Of Anxiety			0.03	
Mild	137 (76.5)	76 (70.4)		
Moderate	30 (16.8)	14 (13)	0.63	0.84 (0.42-1.68)

TABLE 4. Continued

	No Pain Or Mild Pain N (%)	Moderate To Severe Pain N (%)	*P* value	OR (95% CI)
Severe	12 (6.7)	18 (16.7)	0.01	2.7 (1.24-5.91)
Intraoperative pain				
Pelvic Adhesions			0.26	
No	111 (62)	74 (68.5)		
Yes	68 (38)	34 (31.5)	0.27	0.75 (0.45-1.24)
The Number Of Trocar			0.03	
Three	72 (40.2)	58 (53.7)		
≥ Four	107 (59.8)	50 (46.3)	0.03	0.58 (0.36-0.94)
Uterine Size			0.9	
Atrophy	20 (11.2)	15 (13.9)		
Normal	17 (9.5)	9 (8.3)	0.52	0.71 (0.25-2.02)
First Trimester Of Pregnancy	67 (37.4)	38 (35.2)	0.48	0.76 (0.35-1.65)
Second Trimester Of Pregnancy	75 (41.9)	46 (42.6)	0.61	0.82 (0.38-1.75)
Bleeding volume			0.05	
≤ 20	101 (56.4)	52 (48.1)		
20-50	44 (24.6)	41 (38)	0.03	1.81 (1.05-3.11)
> 50	34 (19)	15 (13.9)	0.66	0.86 (0.43-1.71)
Operative time			0.72	
≤ 120 min	141 (78.8)	87 (80.6)		
> 120 min	38 (21.2)	21 (19.4)	0.72	0.90 (0.49-1.63)
Postoperative pain				
Post-Operative Nausea And Vomiting			0.5	
No	118 (65.9)	77 (71.3)		
Only Nausea	20 (11.2)	8 (7.4)	0.27	0.61 (0.26-1.46)
Vomiting	41 (22.9)	23 (21.3)	0.61	0.86 (0.48-1.54)
Time Of Pelvic Drainage			0.94	
One Day	139 (77.7)	85 (78.7)		
Two Days	30 (16.8)	18 (16.7)	0.95	0.98 (0.52-1.87)
Three Days Or More	10 (5.6)	5 (4.6)	0.72	0.82 (0.27-2.47)
The Indwelling Catheter Time			0.09	
NO or One Day	35 (19.6)	11 (10.2)		
Two Days	70 (39.1)	44 (40.7)	0.08	2 (0.92-4.34)
Three Days Or More	74 (41.3)	53 (49.1)	0.04	2.28 (1.06-4.89)
Volume of pelvic drainage in 24 h			0.44	
≤ 50	65 (36.3)	40 (37)		
50-100	58 (32.4)	28 (25.9)	0.43	0.78 (0.43-1.43)
> 100	56 (31.3)	40 (37)	0.61	1.16 (0.66-2.04)

Values are presented as n (%);
OR, odds ratio; CI, Confidence interval;
Binary logistic regression analysis.

Variables as potential risk factors for acute postoperative pain were identified based on available literature. Preoperative variables were age, BMI, education, occupation, exercise habit, individual disease history, obstetrical history, previous surgical history, history of preoperative chronic pain, type of medical insurance, main indication for surgery, and anxiety level. Data of patient's characteristics were obtained by interview on the day before surgery.

Patient's age, height and weight, occupation, vital signs, obstetrical history, individual disease history, and surgical history were obtained by review of the medical record, and the data were verified for accuracy by staff who conducted preoperative interview. BMI was categorized dichotomously with cutoff at 24 [21, 22]. Subjects were classified by dichotomous variable according to previous major surgery with or without abdominal surgery.

In addition, history of pre-existing pain was assessed, which included aspects of its location, duration, and intensity. Patients who experienced pain for a period of > 3 months at ≥ 15 days per month with intensity of ≥ 2 on an 11-point NRS by preoperative interview were considered to have pre-existing chronic pain [23]. In the questionnaire, preoperative pain was classified according to the location of pain such as the head, cervical vertebra, waist, back, chest, abdomen, and limbs [24].

2.4 Anesthesia, surgical procedures and analgesia

In all patients, similar regimens of general anesthesia and prophylactic analgesia were administered without any premedication on the day of surgery. Patients were monitored with standard procedure by bispectral index (BIS) for depth of anesthesia. General anesthesia was induced with a combination of sulfentanyl (0.4 μg.kg^{-1}) and propofol (2-3 mg.kg^{-1}). Next,

TABLE 5. Univariate analysis of risk factors of acute postoperative somatic pain

	No Pain Or Mild Pain N (%)	Moderate To Severe Pain N (%)	*P* value	OR (95% CI)
Preoperative variable				
Age			0.07	
≤ 45	56 (25.1)	24 (37.5)		
45-55	131 (58.7)	35 (54.7)	0.13	0.62 (0.34-1.14)
> 55	36 (16.1)	5 (7.8)	0.04	0.32 (0.11-0.93)
Medical Insurance Type			0.56	
No	16 (7.2)	7 (10.9)		
New Type Of Rural Cooperative	156 (70)	39 (60.9)	0.25	0.57 (0.22-1.48)
Urban Residents	7 (3.1)	3 (4.7)	0.98	0.98 (0.19-4.94)
Urban Workers	44 (19.7)	15 (23.4)	0.65	0.78 (0.27-2.26)
Education			0.49	
Illiteracy	52 (23.3)	19 (29.7)		
Primary School	97 (43.5)	26 (40.6)	0.37	0.73 (0.37-1.45)
Middle And High School	58 (26)	17 (26.6)	0.57	0.8 (0.38-1.7)
College And Higher	16 (7.2)	2 (3.1)	0.18	0.34 (0.07-1.63)
Occupation			0.002	
No	143 (64.1)	27 (42.2)		
Yes	80 (35.9)	37 (57.8)	0.002	2.45 (1.39-4.32)
Hypertension			0.10	
No	171 (76.7)	55 (85.9)		
Yes	52 (23.3)	9 (14.1)	0.12	0.54 (0.25-1.16)
Diabetes			0.06	
No	207 (92.8)	63 (98.4)		
Yes	16 (7.2)	1 (1.6)	0.13	0.21 (0.03-1.58)
A History Of Abdominal Surgery			0.001	
No	176 (78.9)	37 (57.8)		
Yes	47 (21.1)	27 (42.2)	0.001	2.73 (1.51-4.94)
Cesarean Section			0.02	
No	202 (90.6)	51 (79.7)		
Yes	21 (9.4)	13 (20.3)	0.02	2.45 (1.15-5.23)
Parity			0.62	
≤ One	69 (30.9)	24 (37.5)		
Two	108 (48.4)	28 (43.8)	0.36	0.75 (0.4-1.39)
> Two	46 (20.6)	12 (18.8)	0.47	0.75 (0.34-1.65)
Abortion			0.26	
≤ One	82 (36.8)	29 (45.3)		
Two	71 (31.8)	14 (21.9)	0.11	0.56 (0.27-1.14)
> Two	70 (31.4)	21 (32.8)	0.62	0.85 (0.44-1.62)
Dysmenorrhea			0.70	
No	144 (64.6)	43 (67.2)		
Yes	79 (35.4)	21 (32.8)	0.70	0.89 (0.49-1.61)
BMI			0.80	
< 24	126 (56.5)	35 (54.7)		
≥ 24	97 (43.5)	29 (45.3)	0.80	1.08 (0.62-1.88)
Main indication for surgery			0.65	
Physical Findings	141 (63.2)	38 (59.4)		
Descensus Uteri	13 (5.8)	2 (3.1)	0.47	0.57 (0.12-2.64)
Changes In Menstruation	51 (22.9)	17 (26.6)	0.53	1.24 (0.64-2.38)
Dysmenorrhea	18 (8.1)	7 (10.9)	0.45	1.44 (0.56-3.71)
Preoperative Chronic Pain			0.39	
No	159 (71.3)	42 (65.6)		
Yes	64 (28.7)	22 (34.3)	0.38	1.3 (0.72-2.35)
Exercise Habit			0.46	
No	168 (75.3)	51 (79.7)		
Yes	55 (24.7)	13 (20.3)	0.47	0.78 (0.39-1.54)
The Level Of Anxiety			0.09	

TABLE 5. Continued

	No Pain Or Mild Pain N (%)	Moderate To Severe Pain N (%)	*P* value	OR (95% CI)
Mild	159 (71.3)	54 (84.4)		
Moderate	38 (17)	6 (9.4)	0.10	0.46 (0.19-1.16)
Severe	26 (11.7)	4 (6.3)	0.16	0.45 (0.15-1.36)
Pelvic Adhesions			< 0.001	
No	156 (70)	29 (45.3)		
Yes	67 (30)	35 (54.7)	< 0.001	2.81 (1.59-4.97)
The Number Of Trocar			0.15	
Three	106 (47.5)	24 (37.5)		
≥ Four	117 (52.5)	40 (62.5)	0.16	1.51 (0.85-2.67)
Uterine Size			0.28	
Atrophy	26 (11.7)	9 (14.1)		
Normal	21 (9.4)	5 (7.8)	0.55	0.69 (0.2-2.37)
First Trimester Of Pregnancy	76 (34.1)	29 (45.3)	0.83	1.1 (0.46-2.63)
Second Trimester Of Pregnancy	100 (44.8)	21 (32.8)	0.27	0.61 (0.25-1.48)
Bleeding volume			0.63	
≤ 20	119 (53.4)	34 (53.1)		
20-50	68 (30.5)	17 (26.6)	0.68	0.87 (0.46-1.66)
> 50	36 (16.1)	13 (20.3)	0.48	1.3 (0.63-2.68)
Operative time			0.52	
≤ 120 min	179 (80.3)	49 (76.6)		
> 120 min	44 (19.7)	15 (23.4)	0.52	1.25 (0.64-2.42)
Post-Operative Nausea And Vomiting			0.97	
No	152 (68.2)	43 (67.2)		
Only Nausea	22 (9.9)	6 (9.4)	0.94	0.96 (0.37-2.53)
Vomiting	49 (22)	15 (23.4)	0.82	1.08 (0.55-2.12)
Time Of Pelvic Drainage			0.17	
One Day	170 (76.2)	54 (84.4)		
Two Days	42 (18.8)	6 (9.4)	0.09	0.45 (0.18-1.12)
Three Days Or More	11 (4.9)	4 (6.3)	0.82	1.14 (0.35-3.74)
The Indwelling Catheter Time			0.35	
NO or One Day	32 (14.4)	14 (21.9)		
Two Days	88 (39.4)	26 (40.6)	0.4	0.45 (0.34-1.54)
Three Days Or More	103 (46.2)	24 (37.5)	0.15	1.14 (0.27-1.22)
Volume of pelvic drainage in 24 h			0.88	
≤ 50	80 (35.9)	25 (39.1)		
50-100	67 (30)	19 (29.7)	0.78	0.91 (0.46-1.79)
> 100	76 (34.1)	20 (31.3)	0.61	0.84 (0.43-1.64)

Values are presented as n (%);
OR, odds ratio; CI, Confidence interval;
Binary logistic regression analysis.

rocuronium (6-8 mg.kg^{-1}) was administered to allow tracheal intubation, and further boluses of rocuronium were administered to maintain the train-of-four at 0-10%. Anesthesia was maintained with oxygen in air (1 : 2), propofol, remifentanil, and sevoflurane. Morphine (0.1 mg.kg^{-1}) and palonosetron (0.25 mg) were administered 30 minutes before the end of the operation when administration of the inhalation anesthesia was stopped. During closure of the skin, remifentanil infusion was discontinued [25], and after closure, 10 mL of 0.75% ropivacaine local anesthesia was infiltrated at the incision site.

All surgical procedures were performed by or under supervision of experienced surgeons according to standard protocol with laparoscopic ports (1 × 10 mm and 2-3 × 5 mm). The uterus was removed vaginally by volume-reducing techniques. During surgery, intra-abdominal pressure was maintained at 12-13 mmHg, and at the end of procedure, CO2 was evacuated by manual compression of the abdomen through the open laparoscopic ports. Intraoperative procedures and diagnosis, duration of operation, bleeding volume, and intraoperative complications were noted.

At the post anesthesia care unit (PACU), patients were titrated with morphine by the anesthesiologist as follows: Level of subjective pain intensity was obtained at 5 minutes' interval, and repeat 1-2 mg bolus dose of morphine was administered until NRS score of < 4/10 was achieved, indicating adequate level of analgesia based on responses of the patients to questions by the anesthesiologist [26].

One hour later, the patients were moved to the ward; if recurrence of NRS score ≥ 4/10 was observed, 50-mg suppository of indomethacin was administered though the rectum, and if the score of ≥ 4/10 persisted, IM pethidine injection was administered to relieve pain [27]. The total amount of

TABLE 6. Multivariate analysis of risk factors of acute postoperative pain

Risk factors	*P* value	OR	95% Confidence interval	
visceral pain				
BMI				
< 24	Reference			
≥ 24	0.046	0.6	0.37	0.99
Main indication for surgery				
Physical Findings	Reference			
Descensus Uteri	0.019	0.09	0.01	0.67
Changes In Menstruation	0.427	1.26	0.71	2.25
Dysmenorrhea	0.363	0.66	0.27	1.62
Post-Operative Nausea And Vomiting				
No	Reference			
Only Nausea	0.086	2.05	0.9	4.65
Vomiting	0.016	2.09	1.15	3.81
low back pain				
BMI				
< 24	Reference			
≥ 24	0.015	0.51	0.30	0.88
Preoperative Chronic Pain				
No	Reference			
Yes	< 0.001	3.61	2.08	6.24
The Level Of Anxiety				
Mild	Reference			
Moderate	0.353	0.70	0.34	1.48
Severe	0.004	3.46	1.50	7.98
The Number Of Trocar				
Three	Reference			
≥ Four	0.009	0.49	0.29	0.84
Somatic pain				
Occupation				
No	Reference			
Yes	0.006	2.28	1.27	4.09
A History Of Abdominal Surgery				
No	Reference			
Yes	0.011	2.25	1.21	4.19
Pelvic Adhesions				
No	Reference			
Yes	0.006	2.31	1.27	4.19

Values are presented as n (%);
OR, odds ratio;
Multivariate logistic regression analysis.

analgesia during postoperative period (including that at PACU) and any adverse events were recorded in each patient.

Pain was assessed by the study team retrospectively on postoperative day 1 and 7 at 17:00 [28], using 11-point NRS for different types of acute postoperative pain according to the method in a previous study for average pain at rest and at movement, and worst pain [12]. For assessment of the predictors of and risk factors for intense pain scores after surgery, we considered that highest pain intensity is generally attained on postoperative day 1, and highest pain scores are

obtained at interview itemizing maximum pain after surgery [15]. Based on these facts, we selected maximum pain during 7 days as the measure of severe postoperative pain in the prediction analysis [23].

2.5 Statistical analysis

In our hospital, every year, approximately 1500 patients undergo LAVH surgery. Based on mean value of maximum acute postoperative pain after LAVH of approximately 4.5 (NRS 0-10), standard deviation of 2, and permissible error ≤ 0.5, in total, 207 patients were required, with expected loss to follow-up of 10%.

Statistical analysis was performed with Stata 15. Baseline data are expressed as mean (SD) for continuous variables, or number of patients (%) for binary or categorical data. Normality was determined using Kolmogorov-Smirnov tests. Box plot or scatter plot was used to detect outliers. Collinearity was examined by variance inflation factor (VIF); according to NRS score, acute postoperative pain was categorized into mild pain and moderate to severe pain [29]. Categorical data were compared using Fisher's exact test. Continuous variables were compared using Student's *t*-test (parametric) and Mann-Whitney U-test (nonparametric). Assumption of linearity was examined using empirical logit plots to preserve degrees of freedom. All variables with *P*-value < 0.20 in univariate analysis were entered into multivariable logistic regression models; those with $P \leq 0.05$ by multivariable logistic regression were considered significant, and the odds ratio (OR), 95% CIs, and *P*-value were reported. Discrimination of the model was quantified by the area under the receiver operating characteristic (ROC) curve [30]. All statistical tests were two-sided, and $P < 0.05$ was considered to be statistically significant.

3. Results

3.1 Study sample

A total of 407 patients were screened, among who, 120 patients were missing complete records or without records: Forty-two (35%) patients were excluded because of change in the mode of surgery, 38 patients did not conform to the inclusion criteria, and three patients (2.5%) were lost to follow-up. Finally, 287 remaining patients with complete baseline data were enrolled. Flowchart of exclusion and loss to follow-up is shown in Fig. 1.

The mean [minimum-maximum] age at the time of inclusion was 49.20 [33-70] years. In the cohort of 287 patients, history of hypertension was noted in 61 patients (21.3%), and diabetes, in only 17 patients (5.9%); history of abdominal surgery, such as cesarean section, hysteromyoma decollement, cholecystectomy or appendectomy was noted in 74 (25.8%) patients [31, 32]. Majority of the patients were without much anxiety on preoperative day 1, and among those, self-report of mild anxiety was obtained in 74.2% patients. In 253 (88.2%) patients, birth was through vaginal route, and in 34 patients (11.8%), it was by cesarean section (Table 1).

3.2 Preoperative pain

In the study cohort, preoperative chronic pain was observed in 84 patients: headache in 23 (8.0%) patients, cervical pain in 13 (4.5%) female patients, low back pain in 46 (16.0%) patients, shoulder pain in four (1.4%) patients, stomachache in one patient, and pain of the limbs in five (1.7%) female patients; in addition, dysmenorrhea was observed in 100 (34.8%) female patients. Nevertheless, no chronic pain was reported by 129 patients before surgery.

Different types of moderate to severe pain ($\geq$ 1 type) were observed in 217 patients: one type in 116 patients, two types in 81 patients, three types in 17 patients, four types in 3 patients. Moreover, no pain or mild pain was reported in 70 patients, which suggests achievement of insufficient analgesia in our cohort.

3.3 Postoperative pain

Among 254 patients with postoperative visceral pain, the pain was located at the middle of the pelvic area in majority of the patients and with moderate to severe degree in 125 women. Within 2 days after surgery, low back pain was reported in 220 patients, of which 108 patients were cases of moderate to severe low back pain, and 11 patients were worst cases of severe low back pain such as spine fracture. After delivery of local anesthesia to the area of the laparoscopic ports, severe somatic pain was revealed in only six patients. Moreover, in our study, shoulder pain was observed in 44 (15.3%) patients (Table 2).

In the total cohort, on postoperative day 1, the mean NRS score of maximum postoperative visceral pain was 3.71, and that of maximum acute postoperative low back pain was 3.17, and no significant difference was observed between the patients with visceral pain and those with low back pain; in addition, the mean NRS score of maximum acute postoperative somatic pain was 1.72. With regard to the pain location/type, visceral pain and low back pain was observed in majority of the patients, followed by somatic pain and shoulder pain.

3.4 Postoperative analgesia

At PACU, analgesics were administered in 35 (12.3%) patients, and maximum pain was 5 on NRS (0-10); particularly, on postoperative day 1, analgesics were administered in 93 (32.4%) patients, and among those, repeat administration of analgesic agent was required in 34 (36.56%) patients. After administration of pethidine, there was no recurrence of serious pain in almost all patients.

3.5 Risk factors of acute postoperative visceral pain

Among 24 potential risk factors included in univariate analysis, six factors were associated with acute postoperative visceral pain with statistical significance ($P < 0.2$): medical insurance type, hypertension, diabetes, BMI, main indication for surgery, and postoperative nausea and vomiting (Table 3). All those combined were submitted to multivariate analysis; in the results, BMI, main indication for surgery, and postoperative nausea and vomiting were associated with acute postoperative

visceral pain ($P < 0.05$) (Table 6).

3.6 Risk factors of acute postoperative low back pain

Among the risk factors of low back pain included in univariate analysis, 11 factors were associated with acute postoperative low back pain with statistical significance ($P < 0.2$): age, medical insurance type, history of abdominal surgery, mode of delivery, BMI, main indication for surgery, preoperative chronic pain, anxiety, the number of trocar, bleeding volume, and the time of indwelling catheter (Table 4). All those combined were submitted to multivariate analysis; in the results, BMI, preoperative chronic pain, anxiety, and the number of trocar were associated with acute postoperative low back pain ($P < 0.05$) (Table 6).

3.7 Risk factors of acute postoperative somatic pain

In the univariate analysis, 10 factors were associated with acute postoperative somatic pain with statistical significance ($P < 0.2$): age, occupation, hypertension, diabetes, history of abdominal surgery, mode of delivery, level of anxiety, pelvic adhesions, the number of trocar, and time of pelvic drainage (Table 5). All those combined were submitted to multivariate analysis; in the results, only occupation, pelvic adhesions, and history of abdominal surgery were associated with acute postoperative somatic pain ($P < 0.05$) (Table 6).

Somatic pain was a significant factor of the length of hospital stay ($P = 0.04$), and visceral pain and somatic pain were significant factors of the increase of the time to get out of bed after surgery (each, $P < 0.01$). Nevertheless, none of the pain types was an influencing factor of the exhaust time ($P > 0.05$).

4. Discussion

Many studies reported the risk factors of postoperative acute pain, but none of those focused on the different types of acute postoperative pain, which may explain the discrepancies of findings among previous studies [14, 33–35]. Our study addresses this limitation, and to the best of our knowledge, it is the first study on risk factors of postoperative acute pain according to different components of pain. Our results indicated that each of various types of acute postoperative pain have unique risk factors, which may explain the inconsistency of risk factors for postoperative pain among the previous studies.

In the LAVH operation, after laparoscopy was established, bipolar electrocoagulation was used to separate and cut off the ovarian proper ligament and the round ligament of uterus in turn. After opening the bladder peritoneal refluxing, vaginal operation was used. Main ligament of uterus, sacral ligament, and uterine artery and vein were cut off by electrocoagulation. The uterus was taken out through vagina and the vaginal stump was sutured with absorbable suture. In laparoscopic total hysterectomy (LTH), the operation is performed under the laparoscope, and there is no vaginal operation except taking out the uterus. LAVH not only broadens the indications of vaginal hysterectomy, especially for patients with pelvic adhesions, but also reduces the difficulty of operation and postoperative complications. This operation perfectly combines the advantages of laparoscopic surgery and vaginal hysterectomy, which greatly reduces the difficulty of operation, shortens the operation time, reduces the amount of bleeding, and is beneficial for postoperative recovery, which was worthy of clinical application.

Prospective observational study revealed the different types of acute postoperative pain; particularly, that after LAVH comprised four types, of which, visceral pain and low pain dominated over somatic pain and shoulder pain. Visceral pain and low back pain caused a major burden to the patients. Kim *et al*. reported inconsistencies of some areas of brain projection between visceral pain and somatic pain [36]. In our study, BMI, main indication for surgery, and postoperative nausea and vomiting were significant factors of acute postoperative visceral pain, BMI, preoperative chronic pain, anxiety, and the number of trocar were significant factors of acute postoperative low back pain, and occupation, pelvic adhesions, and history of abdominal surgery were significant factors of acute postoperative somatic pain.

In our study, 86 (30%) patients reported preoperative chronic pain in ≥ 1 areas, in agreement with data of other studies [37–39]; the majority of patients with preoperative chronic pain reported low back pain, which indicates that preoperative chronic pain was associated with an increased risk of acute low back pain. Patients who experienced chronic severe pain before the operation could easily experience adverse cognition of catastrophic pain, and these patients are usually not willing to get out of bed early; moreover, they may experience more severe postoperative low back pain [40], and preoperative chronic pain can cause central sensitization, which leads to decrease of the pain threshold and increase of the pain sensitivity [40, 41].

The number of trocars was significantly related to acute postoperative low back pain, which conflicts with the fact that the patients undergoing laparoscopic surgery with smaller incision experienced significantly less pain [42]. We observed that the number of trocars is a protective factor, and greater number of trocars increases the difficulty of surgery, for which patients prepare psychologically. Patients in the group with higher number of trocars achieved shorter operation time, without significance as compared to those in the group with lower number of trocars.

BMI was a protective factor against visceral pain and low back pain, which may be due to three reasons: First, obese patients have a larger proportion of subcutaneous fat, which reduces exposure of the nerve endings and consequently, reduces sensitivity to pain [43]; second, as compared with individuals with normal weight, obese patients have lower activity and workload, which supports our observation of lower incidence of joint strain before operation in the patients with obesity; third, medical staff are easily alerted when surgery is planned for obese patients, because of the challenges of the operation.

Severe preoperative anxiety was a risk factor for acute postoperative low back pain, in agreement with the findings of previous studies [23, 44]. However, only 30 patients in our study showed severe preoperative anxiety and needed sedative pills before surgery. Nevertheless, our study provides data for future study on the risk factors of different types of pain

in patients with higher anxiety, such as those with malignant tumors undergoing laparoscopic surgery.

Surgical stress activates neuroendocrine and immunological pathways, and evokes inflammatory responses, which leads to pelvic adhesions and persistent chronic postoperative pain [45, 46]. In our study, history of abdominal surgery (P = 0.22) and pelvic adhesion (P = 0.49) were not associated with preoperative chronic pain; this result could be due to the fact that low back pain was the main component of preoperative chronic pain in the present study. However, history of abdominal surgery was significantly correlated with pelvic adhesion ($P < 0.01$), which is consistent with the results of our previous studies [47, 48]. Both history of abdominal surgery and pelvic adhesion were associated with somatic pain (Table 6). In the assessment of the potential risk factors of different types of pain, since the factor of pelvic adhesions is associated with an increased risk of operative complications, such as injury of the bladder, bowels, and blood vessel [49], we did not delete any of those factors in the analysis.

Almost half of the patients were housewives without other occupation and they experienced more leisure than those who were employed in the workforce; during work, sitting or standing for long periods could lead to fatigue and chronic pain [50, 51]. Our research revealed that occupation was associated with somatic pain, which supports that occupation is a risk factor of pain based on earlier reports [52, 53].

Anatomically, the phrenic nerve (C3-5) innervates the diaphragmatic pleural surface and connects with the supraclavicular nerve (C3-4), which relays sensory input of the acromium process, and irritation of the diaphragm leads to shoulder pain [54, 55]. Shoulder pain after TLH may increase in intensity by intraoperative position and external compression [15]. Trendelenburg position was associated with injury of the shoulder [56]. In the present study, the risk factors of shoulder pain are not reported in the results, but the incidence of shoulder pain was lower as compared with that of previous study; 44 women with postoperative shoulder pain were included, which may influence the accuracy of our results. Study including a large population is needed to confirm the present result of the risk factors of shoulder pain.

To the best of our knowledge, this is the first study to divide acute postoperative pain into four components of visceral pain, somatic pain, shoulder pain, and low back pain, and analyze the risk factors of different types of pain, which is an important strength; the results obtained may provide foundation data for multimode analgesia and positive guidance for prevention and treatment of pain. Nevertheless, our study has some limitations. First, factors related to specific type of surgery and sub-set of population were assessed, and since the population was not global, the findings have restricted applicability. Second, only women were included, despite the fact that sex is an influencing factor of postoperative pain. In future study, different surgery types and populations with larger size should be included. Finally, the risk factors of shoulder pain are not clear, and more samples should be collected for analysis.

5. Conclusions

Acute postoperative visceral pain and low back pain after LAVH are important issues; future studies on visceral pain and low back pain with analgesia administration after LAVH are needed. Different types of acute pain after LAVH are correlated with preoperative, intraoperative, and postoperative factors, and each of the different types of acute postoperative pain have unique risk factors. This study found that patients with severe preoperative anxiety, preoperative chronic pain, less use of trocar or low BMI patients undergoing LAVH surgery are more likely to have moderate and severe low back pain. Clinicians should pay attention to the preoperative education of such patients, relieve preoperative anxiety and control the level of preoperative chronic pain, which is helpful to reduce postoperative acute low back pain. Moderate and severe visceral pain is easy to be found in patients with menstrual disorders, postoperative nausea and vomiting, and low BMI. Therefore, it is necessary to prevent the occurrence of postoperative nausea and vomiting, especially those with menstrual disorders. Secondly, we should analyze the causes of postoperative pain and give appropriate intervention. Only in this way can we reduce the incidence of postoperative acute pain and improve the quality of life. This finding increases present level of understanding of acute postoperative pain, and enables prediction of postoperative pain intensity and precise treatment by clinicians.

ABBREVIATIONS

BMI, body mass index; COX, cyclo-oxygenase; LAVH, laparoscope-assisted vaginal hysterectomy; LBP, low back pain; NRS, numerical rating scale; PACU, post anesthesia care unit; VAS, visual analogue scale; VIF, variance inflation factor.

AUTHOR CONTRIBUTIONS

Luping Huang, MD, and Sijia Chen designed the study, conducted the study, analyzed the data, and approved the final manuscript. Yunchang Mo and Wenwen Du designed the study and wrote the manuscript. Wenwen Du conducted the study. Yunchang Mo and Sijia Chen analyzed data and wrote and edited the manuscript. Sijia Chen and Wenwen Du contributed equally to this work and should be considered co-first authors.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This prospective, observational cohort study was approved by the Ethics Committee (2019-030) in Clinical Research of the First Affiliated Hospital of Wenzhou Medical University and was registered at China Clinical Trial Registry: ChiCTR-ROC-17013036.

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CONFLICT OF INTEREST

The author reports no conflicts of interest in this work.

DATA AVAILABILITY

The clinical data used to support the findings of this study are available from the corresponding author upon reasonable request.

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