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Summary

The mediating role of pain catastrophizing in the relationship between presurgical anxiety and acute postsurgical pain after hysterectomy

Q4 This is the first study showing that it is not presurgical anxiety per se that predicts postsurgical pain intensity, but rather anxiety fully mediated through pain catastrophizing.

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The mediating role of pain catastrophizing in the relationship between presurgical anxiety and acute postsurgical pain after hysterectomy

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A B S T R A C T

The aim of this study was to examine the joint role of demographic, clinical, and psychological variables as predictors of acute postsurgical pain in women undergoing hysterectomy due to benign disorders. A consecutive sample of 203 women was assessed 24 hours before (T1) and 48 hours after (T2) surgery. Baseline pain and predictors were assessed at T1 and postsurgical pain and analgesic consumption at T2. Several factors distinguished women who had no or mild pain after surgery from those who had moderate to severe pain, with the latter being younger, having more presurgical pain, and showing a less favorable psychological profile. Younger age (odds ratio [OR] = 0.90, $P < .001$), presurgical pain (OR = 2.50, $P < .05$), pain due to other causes (OR = 4.39, $P = .001$), and pain catastrophizing (OR = 3.37, $P = .001$) emerged as the main predictors of pain severity at T2 in multivariate logistic regression. This was confirmed in hierarchical linear regression ($\beta = -0.187$, $P < .05$; $\beta = 0.146$, $P < .05$; $\beta = 0.136$, $P < .05$; $\beta = 0.245$, $P < .01$, respectively). Presurgical anxiety also predicted pain intensity at T2. Findings revealed an integrative heuristic model that accounts for the joint influence of demographic, clinical, and psychological factors on postsurgical pain intensity and severity. In further mediation analysis, pain catastrophizing emerged as a full mediator between presurgical anxiety and postsurgical pain intensity. The potential clinical implications for understanding, evaluating, and intervening in postsurgical pain are discussed.

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1. Introduction

Hysterectomy is one of the most common surgeries in women. In Portugal, approximately 11,000 hysterectomies are performed annually; in the United States, around 600,000 hysterectomies are performed yearly [50]. Acute pain is the most common anticipated and expected problem after surgery [1,84], and it is a predicted physiological response to a noxious chemical, thermal, or mechanical stimulus associated with surgery, trauma, and acute illness [11]. Patients submitted to the same surgical procedures report different levels of pain and show different analgesic needs [59,71], because pain is not only a primitive sensory message of tissue trauma, but also a complex psychological experience [61]. Psychological states can either exacerbate or inhibit nociception and the experience of pain through descending modulatory pathways [72,89]. The gate control theory [58], as well as the neuromatrix theory [57] of pain, recognized that pain is a multidimensional subjective experience consisting of complex interactions between sensory-discriminative, motivational-affective, and cognitive-evaluative dimensions.

A recent systematic review [42] suggested that preexisting presurgical pain, anxiety, age, and type of surgery were the 4 most significant predictive factors for postsurgical pain intensity. Pain catastrophizing and preexisting chronic pain were also indicated as significant predictors for postsurgical pain. More recently, the Australian and New Zealand College of Anesthetists [53] recognized that presurgical anxiety, catastrophizing, neuroticism, and depression were associated with higher postsurgical pain intensity.

Acute postsurgical pain creates needless suffering, puts patients at risk of increased postoperative morbidity and mortality, and increases hospital stay and costs of care [39,78]. Overall, it may have

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detrimental effects in both physiological and psychological domains [15,33]. Physiologically, it can impact the metabolic [3,49], immune [18,53], cardiovascular [18], gastrointestinal (due to pain medication, especially opioids) [49], and other systems [18,32,40,74], with higher rates of complications and associated costs [22,41]. Psychologically, it is associated with higher levels of distress, with increasing anxiety, inability to sleep, a feeling of helplessness, loss of control, and inability to think and interact with others [19]. These effects may alter pain perception [53] and initiate a vicious cycle that might result in chronic pain development [53,65,77,79]. In sum, acute postsurgical pain can be considered a major clinical, economic, human, and social problem [30,84]. Thus, it is important to augment knowledge on predictors and potentially modifiable determinants of acute postsurgical pain to facilitate early identification of and intervention in patients at risk.

Little is known about the joint contribution of demographic, psychological, and surgical factors [42] as predictors of pain after surgery. Moreover, relatively few studies have sought to find predictors of acute postsurgical pain experience after hysterectomy [8,38,45]. Most studies in this area focused on the emotional and sexual impact of undergoing this surgery [2,24,28,31,80], and others have addressed the development of chronic pain after hysterectomy [7,82,83].

The aim of this study was to examine the independent and joint contributions of demographic, clinical, and psychological variables as predictors of acute postsurgical pain in women undergoing hysterectomy due to benign causes. Potential direct and mediation effects of psychological predictors were explored.

2. Methods

2.1. Participants and procedure

This study was conducted in a central hospital in northern Portugal. Procedures were approved by the Hospital Ethic Committee. This was a prospective cohort study, with 2 assessments (T1 and T2) performed between March 2009 and September 2010. After written informed consent was obtained from all participants, a consecutive sample of 203 women undergoing hysterectomy was enrolled in the study (all invited participants accepted). Inclusion criteria were age between 18 and 75 years and the ability to understand consent and questionnaire materials. Exclusion criteria were existing diagnoses of psychiatric or neurologic pathology (e.g., dementia) and undergoing hysterectomy due to malignant conditions. Emergency hysterectomies were also excluded due to procedural reasons.

Women were initially assessed 24 hours before (T1) and 48 hours after (T2) surgery, at the hospital. Follow-up assessments were performed by telephone, 4 months and 12 months later; these data, reporting to pain chronification, will be presented elsewhere. From T1 to T2, 8 women were lost to follow-up (3.94%) due to canceled surgery (n = 3), early discharge from hospital (n = 2), unavailability during postsurgical assessment (n = 1), or review of surgical procedure during surgery (oophorectomy, n = 1; myomectomy, n = 1). The remaining 195 women constituted the data analyses sample. The sociodemographic and clinical characteristics of the sample are presented in Table 1. Mean age was 51.0 years (SD = 9.22), 124 (63.6%) women had 4 years or less of formal education, and 60 (30.8%) lived in a rural setting.

2.2. Measures

Before the study, all instruments and study procedures were piloted in a sample of 20 women for evaluation of their feasibility. Those women underwent hysterectomy at the same hospital in which the present study was conducted, and presented similar sociodemographic and clinical characteristics as the study sample.

2.2.1. Presurgical assessment—predictive measures

Upon hospital admission, 24 hours before surgery (T1), the following baseline questionnaires were administered, in a face-to-face interview by a trained psychologist.

2.2.1.1. Sociodemographic and clinical data questionnaire. This questionnaire included questions on age, education, residence, marital status, professional status, household and parity, previous pain, pain due to other causes, previous surgeries, height, weight, menopause, diagnosis/indication for hysterectomy and disease onset, as well as the use of psychotropic drugs.

2.2.1.2. Brief Pain Inventory—Short Form. Used with those patients presenting presurgical pain, the Brief Pain Inventory—Short Form (BPI-SF) [17] measured pain intensity on an 11-point numerical rating scale (from 0 or "no pain" to 10 or "worst pain imaginable"), pain analgesics, perception of analgesics relief (0 to 100%), pain interference in daily activities (general activity, mood, walking, work, relations with others, sleep and enjoyment of life, 0 to 10 scale), and pain location. In this study, the internal consistency reliability [20] (see later) for the pain interference subscale scores was very high ($\alpha = 0.93$).

2.2.1.3. Hospital Anxiety and Depression Scale. The Hospital Anxiety and Depression Scale (HADS) [91] consists of two 7-item subscales that measure anxiety (HADS-A) and depression (HADS-B) levels among patients in nonpsychiatric hospital settings. Item response format is a Likert scale ranging from 0 to 3. Subscale scores vary between 0 and 21. Higher scores represent higher levels of anxiety and depression. In the current sample, internal consistency reliability [20] was adequate for both anxiety (T1: $\alpha = 0.79$) and depression (T1: $\alpha = 0.79$).

2.2.1.4. Pain Catastrophizing Scale of the Coping Strategies Questionnaire—Revised Form. The Pain Catastrophizing Scale of the Coping Strategies Questionnaire—Revised Form (CSQ-R) [75] subscale has 6 items that assess pain catastrophizing. Items were rated on a 5-point adjective rating scale (1 = never, 2 = almost never, 3 = sometimes, 4 = almost always, and 5 = always) rather than the 7-point scale used in the original instrument, due to difficulties expressed by pilot study patients in discriminating the 7 points. To generate the total scale score, the sum of the item scores was divided by the number of items. Scale scores vary between 1 and 5, with higher scores indicating greater use of the specific coping strategy. In the current sample, the Cronbach alpha internal consistency reliability coefficient [20] was 0.87, indicating good reliability.

2.2.2. Surgical procedure and anesthetic technique

Clinical data related to surgery and to anesthesia were retrieved from medical records. From the 195 women who underwent surgery, 142 (72.8%) were submitted to total abdominal hysterectomy, 34 (17.4%) to vaginal hysterectomy, 13 (6.7%) to total abdominal laparoscopic hysterectomy, and 6 (3.1%) had laparoscopically assisted vaginal hysterectomy. Concomitant procedures, such as oophorectomy, ovarian cystectomy, salpingectomy, cystoscopy, or vaginal repair, were also performed in some patients; however, this refined distinction was not considered for the purpose of our study analyses. In abdominal hysterectomies (n = 142), abdominal incision was indicated as being Pfannenstiel (n = 119) or vertical (n = 23), with the former being the first usual choice and the latter being performed just in cases of existence of a previous vertical surgical scar and in exploratory laparotomy. For all women, uterus

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Table 1
Differences between acute pain severity groups (T2) on sociodemographic and clinical characteristics and psychological measures (T1).

Patient characteristics	Total sample (N = 195)	Absence of pain or mild pain (n = 65)	Moderate to severe pain (n = 130)	*P*
Sociodemographic				
Age (y)	51.0 (9.22)	55.4 (10.6)	48.7 (7.5)	<.001
Marital status (married)	167 (85.6%)	55 (84.6%)	112 (86.2%)	NS
Parity	2.04 (1.20)	2.12 (1.23)	2.00 (1.18)	NS
Education (⩽4 y education)	124 (63.6%)	43 (67.2%)	81 (62.3%)	NS
Residence (urban setting)	60 (30.8%)	21 (32.3%)	39 (30.2%)	NS
Professional status (employed)	96 (49.2%)	30 (46.2%)	66 (50.8%)	NS
Clinical—general indicators				
Premenopausal	129 (66.2%)	30 (46.2%)	99 (76.2%)	<.001
Disease onset (mo)	38.8 (52.5)	38.5 (55.4)	39.0 (51.1)	NS
BMI (kg/m^2)	28.6 (4.50)	28.6 (4.44)	28.6 (4.55)	NS
Previous surgeries	137 (70.3%)	42 (64.6%)	95 (73.1%)	NS
Psychotropic use	64 (32.8%)	23 (36.5%)	41 (34.9%)	NS
Clinical—presurgical pain indicators				
Presurgical pain (yes)	118 (60.5%)	28 (43.1%)	90 (69.2%)	<.001
Intensity (worst level)	3.12 (3.20)	2.41 (2.58)	4.49 (3.19)	<.001
Intensity (average level)	2.11 (2.13)	1.17 (1.64)	2.58 (2.20)	<.001
Presurgical analgesic use	58 (29.7%)	9 (13.8%)	49 (37.7%)	.001
Pain total interference (0–10)	1.29 (1.85)	0.80 (1.62)	1.45 (1.90)	NS
Pain due to other causes	125 (64.1%)	33 (50.8%)	92 (70.8%)	.001
Psychological measures				
HADS: anxiety	7.29 (4.42)	5.65 (3.48)	8.12 (4.62)	<.001
HADS: depression	2.35 (3.04)	1.68 (2.22)	2.69 (3.33)	<.05
CSQ-R: pain catastrophizing	1.80 (0.90)	1.43 (0.61)	1.99 (1.00)	<.001

Continuous variables are presented as mean (SD); categorical variables are presented as n (%).
BMI = body mass index, CSQ-R = Coping Strategies Questionnaire, Revised, HADS = Hospital Anxiety and Depression Scale, T1 = 24 hours before surgery, T2 = 48 hours after surgery.

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weight and height were also recorded. The type of anesthesia was classified as general (n = 57, 29.2%), locoregional (n = 24, 12.3%) or combined (general plus locoregional; n = 114, 58.4%), and the American Society of Anesthesiologists score (physical status classification of the American Society of Anesthesiologists) was recorded, including cases of American Society of Anesthesiologists grade I (58, 29.7%), II (123, 63.1%) and III (14, 7.2%).

2.2.3. Postsurgical assessment

2.2.3.1. Primary outcome measure: acute postsurgical pain. Women were asked to rate their worst and average pain level within the first 48 hours after surgery, on an 11-point numerical rating scale (from the BPI-SF), already described.

2.2.3.2. Clinical measures. Clinical data related to surgery, anesthesia, and analgesia were obtained from medical records. Information about type of hysterectomy and uterus weight and height was registered. Concerning anesthesia, the type of anesthesia and American Society of Anesthesiologists score were also gathered. Furthermore, information about the use of psychotropic drugs during hospital stay as well as the duration of hospital length were collected. In addition to the 11-point pain rating scale women were assessed on analgesic relief using the scale from 0 to 100%, from the BPI-SF [17].

All patients were assigned to an individualized standardized 48-hour analgesia protocol that was determined and supervised by the Acute Pain Service and established before transferring the patient to the infirmary. Delivery of the analgesic protocol was either epidural or intravenous. The standardized epidural protocols could be: (1) a continuous epidural infusion (delivered infusion balloon) with ropivacaine (0.1%) and fentanyl (3 μg/mL); or (2) administration of an epidural morphine bolus (2 to 3 mg, 12/12 hours). The intravenous protocol was composed by a continuous intravenous infusion (delivered infusion balloon) of tramadol (600 mg), metamizol (6 g), and metoclopramide (60 mg). Paracetamol (1 g 6/6 hours) and nonsteroidal anti-inflammatory drugs (ketorolac 30 mg 12/12 hours or parecoxib 40 mg 12/12 hours) were always included as coadjuvant analgesics. All analgesic regimens included prokinetic treatment that was standardized to metoclopramide (10 mg intravenously 8/8 hours). All protocols had indications for the prescription of rescue analgesics beyond the standardized analgesic protocol given moderate to severe acute postsurgical pain levels (NRS ⩾ 4). Because of the great variability in analgesics' medications and dosages, no attempt was made to determine total equianalgesic medication dosages. It was rather recorded whether rescue analgesics were given to patients.

2.3. Statistical analyses

The software G Power, version 3.1.2 [27], was used to investigate the sample size required to test the proposed effects. With 147 participants, there would be 95% power to detect an effect size of 0.15 (medium effect size), assuming a type I error of 5% and 6 predictors included in the linear regression analysis. Based on previous studies conducted by the team with a similar sample [67], we expected a 15% attrition rate from T1 to T2. Therefore, collecting 169 patients would be sufficient to assure statistical power. Given that this is part of a larger prospective cohort study (4 time points), a total of 203 patients were included in the study.

Data were analyzed using the Statistical Package for the Social Sciences, version 18.0 (SPSS, Inc., Chicago, Illinois, USA). Internal consistency of responses to the questionnaires was assessed using Cronbach alpha [20]. The outcome variable in this study is "worst level of acute postsurgical pain" either assessed as a dichotomous variable (pain severity) or as a continuous variable (pain intensity; NRS 0 to 10). For the dichotomous outcome, patients were classified into 2 groups, no or mild pain (NRS ⩽ 3 for "worst pain level") and moderate to severe pain (NRS ⩾ 4 for "worst pain level"). The selected cut-point was based on: (1) the specific analgesic procedures of the hospital, which state that an NRS value of ⩾4 determines further administration of rescue analgesics; (2) recommendations from other studies suggesting that this threshold determines distinct acute pain consequences with higher levels of functional limitation when a patient states pain of level 4 or more [5,23,26,36].

Both *t* tests (for continuous variables) and χ^2 tests (for nominal variables) were performed to compare demographic, clinical, and psychological measures between patients with and without moderate or severe pain 48 hours after surgery. Furthermore, Pearson correlation coefficients were also calculated among study variables to determine the predictor variables to include in the regression analyses.

Logistic regression analyses were conducted to determine risk factors for the presence of moderate to severe pain, using pain severity as outcome. Multiple linear regression analyses were performed to identify significant predictors for worst postsurgical pain intensity as outcome. The variables included in both regression analyses were either the ones that were found to distinguish between the 2 pain groups ($P \leqslant .001$) or those that showed a strong association with worst pain intensity ($P < .001$). Additionally, univariate regression analyses, along with findings of previous studies [13,35,42,47,48] assisted in the final selection for multiple and logistic hierarchical regression models. To control for the influence of multicollinearity, we calculated the variance inflation factor value for every independent variable. The variable was included if variance inflation factor was <3. The option to use both logistic and linear regression to investigate the predictors of acute postsurgical pain is related to an interest in both pain severity (cut-point with clinical implications) and intensity as outcomes variables. A replication of findings via these 2 procedures will reinforce their robustness.

For mediation analysis, and to circumvent recognized issues with the Baron and Kenny method and the Sobel test for testing mediation [55], the Preacher and Hayes (2008) bootstrapping methods [69] were used for testing indirect effects. To test for mediation, a distinction between the various effects and their corresponding weights was performed (Fig. 1). The total effect of presurgical anxiety on postsurgical pain intensity (weight *c*) consists of both a direct effect of presurgical anxiety on postsurgical pain intensity (weight *c′*), and also an indirect effect of presurgical anxiety on postsurgical pain intensity through a mediator, that is, pain catastrophizing (weight *ab*). The effect of presurgical anxiety on pain catastrophizing is represented by weight *a*, whereas weight *b* is the effect of pain catastrophizing on postsurgical pain intensity. To assess this indirect effect, a bootstrapping method was used following the procedure described by Preacher and Hayes [37,69]. Specifically, point estimates and 95% bias-corrected and accelerated bootstrapped confidence intervals were estimated with 5000 bootstrap resamples.

3. Results

3.1. Sociodemographic, clinical, and psychological characteristics

Sixty-five women reported no or mild pain (NRS $\leqslant$ 3) after surgery, whereas 130 reported moderate to severe pain (NRS $\geqslant$ 4). Table 1 shows sociodemographic and clinical characteristics of both the total patient sample and those of each postsurgical pain severity group (NRS $\leqslant$ 3 and NRS $\geqslant$ 4). Apart from age, the groups did not differ significantly on any of the sociodemographic measures. Aside from being younger ($t = 4.55$, $P < .001$), women with moderate to severe postsurgical pain were also more likely to be premenopausal ($\chi^2 = 17.42$, $P < .001$) and to present more presurgical pain either related to the illness underlying surgery ($\chi^2 = 12.41$, $P < .001$) or to other causes ($\chi^2 = 7.56$, $P = .001$) (Table 1). Furthermore, these women showed a worse psychological profile (Table 1), revealing more anxiety ($t = -4.17$, $P < .001$), depression ($t = -2.53$, $P < .05$), and pain catastrophizing ($t = -4.90$, $P < .001$) (Table 1).

Regarding the impact of surgery, abdominal hysterectomy was more significantly associated with moderate to severe pain than vaginal hysterectomy ($\chi^2 = 10.63$, $P = .001$) (Table 2). The groups did not show any difference on other clinical parameters such as uterus weight and height, type of anesthesia, or type of analgesia (Table 2). Additionally, 48 hours after surgery (T2), women with moderate to severe pain were given more rescue analgesics ($\chi^2 = 32.19$, $P < .001$) than women with no or mild postsurgical pain (Table 2).

3.2. Risk factors for postsurgical pain severity

To determine the risk factors associated with postsurgical pain severity, a logistic regression was conducted (Table 3), with the dichotomous pain severity scores as outcome (2 pain groups: no or mild pain, NRS $\leqslant$ 3, versus moderate to severe pain, NRS $\geqslant$ 4). Age was included in the first step, and the type of hysterectomy was entered in the second step due to its significance in previous analyses. Presurgical pain (absent, present) was entered along with pain due to other causes (absent, present) in the third step. In the fourth and fifth steps, anxiety and pain catastrophizing were added, respectively, as the psychological variables expected to have the largest impact on postsurgical pain, taking into account either previous univariate analyses or results from other studies [13,35,42,47,48]. As shown in Table 3, the variables that emerged as predictors of pain severity in the final model were age (OR = 0.90, 95% confidence interval [CI] 0.86 to 0.95, $P < .001$), presurgical pain (OR = 2.50, 95% CI 1.12 to 5.60, $P < .05$), pain due to other causes (OR = 4.39, 95% CI 1.83 to 10.5, $P = .001$), and pain catastrophizing (OR = 3.37, 95% CI 1.63 to 6.95, $P = .001$), with younger women and those presenting increased level of the other 3 characteristics having a higher probability of being in the moderate to severe pain group. The type of hysterectomy and presurgical anxiety were not significant predictors in the final model. However, presurgical anxiety was a significant predictor in step 4, before being corrected for pain catastrophizing (OR = 1.09, 95% CI 1.00 to 1.19, $P < .05$). After pain catastrophizing was entered on step 5, presurgical anxiety was no longer significant (OR = 0.96, 95% CI 0.86 to 1.08, not significant).

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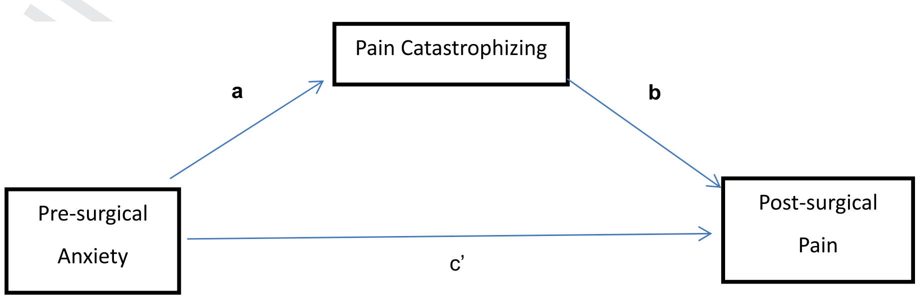

Fig. 1. Graphic representation of the mediation model. Note that the total effect (weight c) consists of a direct effect (weight c′) and the indirect effect (ab weight).

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Table 2
Differences between acute pain severity groups on postsurgical, anesthetic, and surgical variables (T2).

Postsurgical data	Total sample (N = 195)	Absence of pain or mild pain (n = 65)	Moderate to severe pain (n = 130)	*P*
Clinical—general indicators				
Type of hysterectomy: abdominal	155 (79.5%)	43 (66.2%)	112 (86.2%)	.001
Uterine weight (g)	208 (204)	177 (216)	223 (196)	NS
Uterine height (cm)	9.48 (2.56)	9.13 (2.43)	9.66 (2.62)	NS
Type of anesthesia: combined	114 (58.5%)	35 (53.8%)	79 (60.8%)	NS
Epidural analgesia	136 (69.7%)	44 (67.7%)	92 (70.8%)	NS
Length of hospital stay (d)	3.12 (1.22)	2.98 (0.75)	3.19 (1.34)	NS
Psychotropic use	73 (37.4%)	26 (40.0%)	47 (36.4%)	NS
Clinical pain and analgesic indicators				
Rescue analgesics	95 (48.7%)	13 (20.0%)	82 (63.1%)	<.001
Percent relief from analgesics (0–100)	92.0 (19.04)	100 (0.0)	88.0 (22.8)	NS

Continuous variables are presented as mean (SD); categorical variables are presented as n (%). Type of hysterectomy: open abdominal and abdominal laparoscopic versus vaginal and vaginal assisted laparoscopic; combined anesthesia (general + loco-regional) versus general anesthesia alone or loco-regional anesthesia alone; epidural analgesia versus intravenous analgesia.
T2 = 48 hours after surgery.

Table 3
Hierarchical logistic regression for risk factors (T1) predicting pain severity, 48 hours (T2) after hysterectomy (n = 188[a]).

Variables	Odds ratio (CI)	*P*
Step 1		
Age[b]	0.92 (0.89–0.96)	<.001
Step 2		
Type of hysterectomy[c]	1.88 (0.85–4.14)	NS
Step 3		
Presurgical pain[d]	1.68 (0.83–3.39)	NS
Pain due to other causes[e]	3.21 (1.58–6.54)	.001
Step 4		
Presurgical anxiety[f]	1.09 (1.00–1.19)	<.05
Step 5 (final model)		
Age[b]	0.90 (0.86–0.95)	<.001
Type of hysterectomy[c]	1.82 (0.72–4.66)	NS
Presurgical pain[d]	2.50 (1.12–5.60)	<.05
Pain due to other causes[e]	4.39 (1.83–10.5)	.001
Presurgical anxiety[f]	0.96 (0.86–1.08)	NS
Pain catastrophizing[g]	3.37 (1.63–6.95)	.001

T1 = 24 hours before surgery; T2 = 48 hours after surgery.
[a] After removing 7 outliers, the final model correctly predicted 76% of all patients.
[b] Continuous variable, in years.
[c] Dichotomous variable: 0 = vaginal, 1 = abdominal.
[d] Dichotomous variable: 0 = no, 1 = yes.
[e] Dichotomous variable: 0 = no, 1 = yes.
[f] Continuous variable: Hospital Anxiety and Depression Scale, anxiety subscale.
[g] Continuous variable: Coping Strategies Questionnaire, Revised (pain catastrophizing subscale).

3.3. Predicting postsurgical pain intensity

Table 4 presents Pearson correlation coefficients between worst postsurgical pain intensity and other study variables. Worst postsurgical pain intensity was significantly correlated with age ($r = -0.29$, $P < .001$) and previous pain intensity ($r = 0.33$, $P < .001$). Worst postsurgical pain was also significantly correlated with psychological measures such as presurgical anxiety ($r = 0.28$, $P < .001$) and pain catastrophizing ($r = 0.35$, $P < .001$). These results were used to determine the set of predictors to include in the regression model.

To determine the predictors of postsurgical pain intensity, a hierarchical linear regression analysis was performed (Table 5). The regression model was the same as previously described for pain severity as outcome (Table 3). Furthermore, we sought to understand and clarify the specific relationship between presurgical anxiety and pain catastrophizing, and postsurgical pain intensity. The results of the hierarchical linear regression analysis, presented in Table 5, showed an initial model that replicates the results obtained for the first 3 steps of the logistic regression (Table 3). On step 4, presurgical anxiety was included and proved to be a significant predictor ($\beta = 0.184$ $P = .009$), explaining an additional 3% of the variance in pain intensity. On the final step, pain catastrophizing was entered, also emerging as a significant predictor ($\beta = 0.245$, $P = .002$), adding 3.9% to the explained variance. However, whereas the other variables were still significant predictors, the contribution of presurgical anxiety was no longer significant ($\beta = 0.048$, $P = .554$). The variance explained by the initial model (first 4 steps) was 20.2%, whereas the variance explained by the final model increased to 24.0%. The inclusion of pain catastrophizing in the model improved the variance explained and seemed to reveal a full mediation effect between anxiety and postsurgical pain. The next analysis explores this potential mediation.

3.4. Mediation analysis

We investigated the mediation hypothesis further using Preacher and Hayes' [69] bootstrapping methods to test for indirect effects. Hence, we tested whether the effect of presurgical anxiety on postsurgical pain was mediated by pain catastrophizing (Fig. 1). Presurgical anxiety was positively and significantly associated with postsurgical pain intensity ($c = 0.19$, SE = 0.05, $P = .0001$) and with pain catastrophizing ($a = 0.12$, SE = 0.01, $P < .0001$). Additionally, pain catastrophizing was positively and significantly related to postsurgical pain intensity ($b = 0.89$, SE = 0.27, $P = .001$).

When pain catastrophizing was tested as a mediator, the direct effect of presurgical anxiety on postsurgical pain intensity became nonsignificant ($c' = 0.09$, SE = 0.06; Fig. 1) and the indirect effect of presurgical anxiety on postsurgical pain (i.e., simple mediation) was significant ($ab = 0.11$, SE = 0.03), as the bootstrapped confidence interval (bias-corrected and accelerated 95% CI: 0.04 to 0.17 with 5000 resamples) excluded zero. These results support the mediation effect of pain catastrophizing between presurgical anxiety and postsurgical pain intensity.

4. Discussion

The present study is, to our knowledge, the first aiming to identify the joint and independent contribution of demographic, clinical, and psychological risk factors for acute postsurgical pain intensity after hysterectomy due to benign disorders. This is also the first study showing the mediating role of pain catastrophizing between presurgical anxiety and postsurgical pain intensity, indicating that it is not presurgical anxiety per se that predicts postsurgical pain intensity, but rather anxiety mediated through pain catastrophizing.

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Table 4
Intercorrelations of age, psychological measures, and pain at T1 and T2.

	1	2	3	4	5	6	7	8	9
1. Age	–	.11	−.25***	−.01	−.11	−.36***	−.27***	−.29***	−.27***
2. Pain, other causes		–	.18*	.009	.24**	.16*	.10	.19**	.21**
3. HADS: anxiety T1			–	.55***	.57***	.15*	.13	.28***	.25***
4. HADS: depression T1				–	.45***	.07	.08	.19**	.22**
5. CSQ-R: pain catastrophizing T1					–	.17*	.12	.35***	.39***
6. Worst pain T1						–	.92***	.33***	.37***
7. Average pain T1							–	.31***	.34***
8. Worst pain T2								–	.73***
9. Average pain T2									–

CSQ-R = Coping Strategies Questionnaire, Revised, HADS = Hospital Anxiety and Depression Scale, T1 = 24 hours before surgery, T2 = 48 hours after surgery.
* $P < .05$.
** $P < .01$.
*** $P < .001$.

Table 5
Hierarchical linear regression analysis for predictors of postsurgical pain intensity, 48 hours after hysterectomy (N = 195).

Variables	t	β	R^2	ΔR^2	ΔF
Step 1			0.085	0.085	17.670***
Age[a]	−4.204***	−0.291			
Step 2			0.100	0.016	3.301
Type of hysterectomy[b]	1.817	0.134			
Step 3			0.172	0.071	8.085***
Presurgical pain[c]	2.131*	0.155			
Pain, other causes[d]	3.047**	0.206			
Step 4			0.202	0.030	7.040**
Presurgical anxiety[e]	2.653**	0.184			
Step 5 (final model)			0.240	0.039	9.484**
Age[a]	−2.526*	−0.187			
Type of hysterectomy[b]	1.183	0.083			
Presurgical pain[c]	2.079*	0.146			
Pain, other causes[d]	2.030*	0.136			
Presurgical anxiety[e]	0.593	0.048			
Pain catastrophizing[f]	3.080**	0.245			

T1 = 24 hours before surgery; T2 = 48 hours after surgery.
* $P < .05$.
** $P < .01$.
*** $P < .001$.
[a] Continuous variable in years.
[b] Dichotomous variable: 0 = vaginal and vaginal assisted laparoscopic, 1 = open abdominal and abdominal laparoscopic.
[c] Dichotomous variable: 0 = no, 1 = yes.
[d] Dichotomous variable: 0 = no, 1 = yes.
[e] Continuous variable, Hospital Anxiety and Depression Scale, anxiety subscale.
[f] Continuous variable, Coping Strategies Questionnaire, Revised (pain catastrophizing subscale).

4.1. Predictors of moderate/severe postsurgical pain after hysterectomy

Several presurgical factors distinguished women who had no or mild postsurgical pain from those who had moderate to severe pain, with the latter being younger, having higher level of presurgical pain, and showing a worse psychological profile in cognitive and emotional evaluations.

Regarding sociodemographic predictors, in both regression analyses (logistic and linear), younger women showed an increased risk for higher postsurgical pain severity and intensity. This replicates results from other studies in which age emerged as a significant predictor, with younger patients reporting more postsurgical pain in cases of breast surgery [43,48], cholecystectomy [4], abdominal surgeries [13], prostatectomy [26], and inguinal hernioplasty [52]. The protective effect of increased age has been related to a reduction in peripheral nociceptive function [66,88]. However, considering the type of surgery (hysterectomy), other factors may contribute to higher pain perception, namely the fear of losing the uterus at a young age and its impact on fertility, body image, and sexuality [2,24,28,29,31,80].

In terms of clinical predictors, abdominal hysterectomies have been associated with higher postsurgical pain than vaginal hysterectomies [44]. Open abdominal surgeries are among the most painful surgical procedures [16,47]. However, in the present study, the surgical route was not a significant predictor of postsurgical pain. This reinforces the relevance of psychological factors when experiencing and dealing with postsurgical symptoms.

The existence of either presurgical pain (related to the causes that required a hysterectomy) or pain due to other causes was shown to be a significant predictor of postsurgical pain, which replicates findings from other studies on breast surgery [48,62], cholecystectomy [87], abdominal surgery [13,47,85], or inguinal hernioplasty [10]. Prolonged pain stimulation has been shown to exacerbate the nociceptive system through mechanisms of peripheral and central sensitization of nociceptors and central nervous system neurons, respectively [51]. It is possible that plastic changes in the nociceptive system and supraspinal pain control system [33,60,68] may contribute to this association between the presence of presurgical and postsurgical pain. For patients who come for surgery and are screened with presurgical pain or other chronic pain states, it is important to offer special care in terms of presurgical intervention focused on pain management and promoting effective pain coping strategies.

Concerning psychological factors, several studies demonstrated that presurgical anxiety is one of the most important predictors of postsurgical pain in a variety of surgical procedures [21,42,45,48,53]. Pain catastrophizing has also been identified as a major predictor of acute pain experience [35,63,64,73,81,86] in a wide range of surgeries, although no study to date has reported its influence on hysterectomy. Additionally, few studies have included and explored both anxiety and pain catastrophizing as predictors of postsurgical pain. Granot and Ferber [35] focused on the specific relationship between presurgical anxiety, pain catastrophizing, and postsurgical pain in patients undergoing hernioplasty (n = 34) and cholecystectomy (n = 4). Their results indicated that pain catastrophizing predicted postsurgical pain intensity after controlling for anxiety. The study explored a potential mediation between these variables, but only a partial mediation was found. To test for mediation, Granot and Ferber [35] used the Baron and Kenny method. This method presents recognized limitations such as low statistical power and the absence of a measure for the strength of the mediated effect [37,54]. Furthermore, this study had a small (n = 38) and heterogeneous sample (34 hernioplasties and 4 cholecystectomies). In a study by Sommer et al. [81] with 217 ear, nose, and throat surgery patients, the investigators concluded that anxiety is not a significant predictor of acute postsur-

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gical pain, whereas pain catastrophizing is. These results seem to contradict previous reports on the determinant role of anxiety on acute pain.

To the best of our knowledge, the present study is the first to explore this mediation in a sample of benign hysterectomy patients. In accordance with the literature [21,42,45,48,53], we found that presurgical anxiety was a significant predictor of postsurgical pain severity and intensity. However, when the effect of presurgical anxiety was corrected for pain catastrophizing, this effect was no longer significant. In the absence of collinearity problems, which might have accounted for the suppression of the effect of presurgical anxiety, the data indicate a mediation effect via pain catastrophizing. The mediation analysis conducted using state-of-the-art bootstrapping methodology supported the mediation hypothesis. We found that the relationship between anxiety and postsurgical pain is fully mediated by pain catastrophizing. Thus, presurgical anxiety seems to be associated with negative cognitions about pain that predict increased postsurgery pain reports. Pain catastrophizing involves magnification of the threat value of pain and generalization of its negative impact, as well as feelings of helplessness and pessimism in the ability to deal with pain [70,86]. This has clinical implications: as presurgical anxiety increases, women will tend to catastrophize more about pain and this will predict increased acute postsurgical pain intensity.

These mediation results might contribute to clarify apparently incongruent data in the relationship between anxiety and pain [6,26,88,90] and answer some of the questions raised by Sommer et al. [81] as well as by Granot and Ferber [35]. The association found between anxiety and pain catastrophizing and the role of the latter in predicting acute postsurgical pain suggest that both emotional and cognitive factors need to be considered in the prevention and management of acute pain, and that intervening in cognitive factors may have a direct impact on pain experience after surgery. These results may also help to clarify why presurgical pharmacological interventions, through the administration of anxiolytic drugs such as benzodiazepines, have not yet proven to be effective in the reduction of postsurgical pain intensity [12,46]. Prescribing large-spectrum anxiolytic drugs seems to miss a key cognitive factor associated with presurgical anxiety, which is pain catastrophizing.

4.2. Limitations of the study

There are some methodological limitations that need to be considered. Postsurgical pain was assessed both in terms of average pain and in terms of worst pain experienced. Only the latter was analyzed here as outcome. Average pain presented a bimodal distribution, which raises issues regarding its accuracy and statistical reliability, and thus we decided not to use it as an outcome variable. Furthermore, sometimes women were not able to understand the concept of average pain, which is more an integrative measure. This could also have affected the accuracy of the measure and might have influenced its final statistical properties and distribution.

The outcome variable, worst level of postsurgical pain, was assessed only 48 hours after surgery. This assessment at 48 hours after surgery was not focused on the pain at that exact assessment time but rather on the worst level of pain perception during the past 48 hours. We might question whether a more regular assessment of pain intensity, such as at 12, 24, and 48 hours after surgery, could describe more accurately the acute postsurgical pain experience.

Finally, this is a single-site and single-country study, and thus the generalization of the conclusions to populations in other countries should be considered with caution. Future studies need to be conducted to analyze whether this effect can be replicated.

4.3. Clinical practice implications

The integrative model presented here reveals the simultaneous influence that demographic, clinical, and psychological factors may have on postsurgical pain. This is a heuristic parsimonious model that may have clinical implications in understanding and evaluating postsurgical pain, and can be applied directly and easily in the presurgical period to women scheduled for hysterectomy. A clinician can quickly assess these variables without the need of a long and complex protocol that would require highly specialized training. By knowing patient age, presurgical pain, presence or absence of pain due to other causes, levels of pain catastrophizing, and presurgical anxiety, clinical practitioners can quickly and pragmatically assess the risk of women undergoing hysterectomy to develop moderate to severe postsurgical pain. In sum, with this practical model, women at risk for increased acute postsurgical pain can easily be identified and targeted with appropriate intervention strategies.

Our study identified 2 factors amenable to change or to active management through psychological presurgical interventions, namely presurgical anxiety and pain catastrophizing. To deal with anxiety, brief cognitive behavior therapy intervention techniques (such as brief relaxation) have been widely used [9,34,76]. Our results shift the focus to the role of cognitive factors in acute postsurgical pain, suggesting that presurgery interventions should address pain catastrophizing cognitions. These interventions delivered before surgery should aim at challenging and substituting the negative cognitive contents associated with pain catastrophizing with positive pain coping self-statements [9,25,34,56,76]. Such an intervention would be easy to implement within the 24-hour period preceding surgery, when women are already in the hospital setting.

Conflict of interest statement

None declared.

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