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Risk Factors for Persistent Postsurgical Pain in Women Undergoing Hysterectomy Due to Benign Causes: A Prospective Predictive Study

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Abstract: Persistent postsurgical pain (PPSP) is a major clinical problem with significant individual, social, and healthcare costs. The aim of this study was to examine the role of demographic, clinical, and psychological risk factors in the development of PPSP after hysterectomy due to benign disorders. In a prospective study, a consecutive sample of 186 women was assessed 24 hours before surgery (T1), 48 hours after surgery (T2), and 4 months after surgery (T3). Regression analyses were performed to identify predictors of PPSP. Four months after hysterectomy, 93 (50%) participants reported experiencing pain (numerical rating scale >0). Age, pain due to other causes, and type of hysterectomy emerged as significant predictive factors. Baseline presurgical psychological predictors identified were anxiety, emotional illness representation of the condition leading to surgery, and pain catastrophizing. Among the identified psychological predictors, emotional illness representation emerged as the strongest. Acute postsurgical pain frequency and postsurgical anxiety also revealed a predictive role in PPSP development. These results increase the knowledge on PPSP predictors and point healthcare professionals toward specific intervention targets such as anxiety (presurgical and postsurgical), pain catastrophizing, emotional illness representations, and acute pain control after surgery.

Perspective: This study found that presurgical anxiety, emotional illness representations, and pain catastrophizing are risk factors for PPSP 4 months after hysterectomy, over and above age and clinical variables. These findings improve knowledge on PPSP and highlight potential intervention targets for healthcare professionals.

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Key words: Hysterectomy, persistent postsurgical pain, anxiety, emotional illness representation, pain catastrophizing.

Hysterectomy is the most common gynecologic surgery performed in women in Western countries.[72] Although acute pain is an anticipated and expected outcome after surgery,[2,81] the development of chronic or persistent postsurgical pain (PPSP) is a common adverse unforeseen outcome.[63] PPSP refers to pain that develops after surgery, persisting for at least 2 months following surgery. Other causes for such pain—ie, malignancy, chronic infection, preexisting pain, recurring disease—must be excluded.[49,51] PPSP is a major clinical problem with significant

individual, social, and healthcare costs.[37,62,77] This often underreported problem is sometimes considered a "silent epidemic"[87] and has recently been recognized as a possible and common consequence of several types of surgeries,[17,49-51] leading to increasing research in this area.[50,76] Incidence rates of PPSP depend on the type of surgery and range from 10 to 60%.[1] The variability in incidence rates might be due to different study designs and methodologies, surgical techniques, selected samples, and PPSP definitions used.

Several individual, presurgical, intrasurgical, and postsurgical factors such as age, type of surgery, previous pain (related and not related to surgery), and acute postsurgical pain[38,48,63,88] have been identified as predictors for the development of PPSP. Moreover, a recent systematic review[30] focusing on psychosocial predictors of PPSP identified presurgical and postsurgical psychological distress and negative emotional states as risk factors for PPSP. Anxiety and depression have emerged as predictors of persistent pain after surgery in some studies,[7,23] but not in others.[83] Strategies of functional or dysfunctional coping with pain, such as pain catastrophizing, have also been examined as potential predictors, but evidence to date is inconclusive.[22,73] A recent systematic review concluded that more high-quality studies are needed, with standardized measures, appropriate follow-up periods, and sufficient power.[30]

Other potentially important but understudied determinants of PPSP are patients' illness perceptions. The Common-Sense Self-Regulation Model[44,45] suggests that in the context of an illness, people tend to develop individual cognitive and emotional illness representations of their illness.[29,43,66] These representations have been shown to explain significant variation in outcomes in a wide range of medical conditions and in response to different treatments.[28,57,66,67] Past studies using this theoretical perspective focused on the associations between illness representations and functional activity, postsurgical adjustment, or surgical recovery, rather than on their relationship with pain outcomes.[46,54,61,67] However, to date, no study has focused on the relationship between illness representations and PPSP.

The present study aimed to examine the joint role of sociodemographic, clinical, and psychological risk factors for the development of PPSP 4 months after hysterectomy for benign causes in order to develop a more comprehensive understanding of possible causes of PPSP and potential targets for psychosocial interventions. We expected that maladaptive coping strategies, higher levels of anxiety, and depression, as well as less adaptive illness representations, would be related to PPSP 4 months after hysterectomy.

Methods

Participants and Procedure

This study was conducted in a central hospital in northern Portugal (Alto Ave Hospital Center). Ethical approval was granted by the Hospital Ethics Committee. This was a prospective study with assessments 24 hours prior to surgery (T1), and 48 hours (T2) and 4 months (T3) after surgery. Assessments were performed between March 2009 and January 2011. A consecutive sample of 203 women undergoing hysterectomy was invited to take part in the study and provided written informed consent. Inclusion criteria were age between 18 and 75 years and the ability to understand consent procedures and questionnaire materials. Exclusion criteria were existing diagnoses of psychiatric or neurologic pathology (eg, dementia) and undergoing hysterectomy due to malign conditions. Emergency hysterectomies were also excluded due to procedural reasons. T1 and T2 assessments took place in hospital, and T3 follow-up assessment was conducted by telephone. Inclusion in each assessment point and the reasons for loss to T2 and T3 is shown using a flowchart (see Fig 1). The final sample comprised 186 women with assessments performed at T1, T2, and T3.

Measures

All instruments and study procedures were piloted at an initial stage with a sample of 20 women for evaluation of their acceptability, feasibility, and comprehensibility. Those women were not included in the final sample. During the study all questionnaires and interviews were conducted by a trained postgraduate psychologist (P.R.P.).

Presurgical Assessment—24 Hours Before Surgery

Upon hospital admission, 24 hours before surgery (T1), the following baseline questionnaires were administered, in a face-to-face interview, where the interviewer read the questions to patients and recorded the answers.

(1) Sociodemographic and Clinical Factors
- Sociodemographic and Clinical Data Questionnaire: included questions on age, height, weight, education, residence, marital status, professional status, household and parity, previous pain (related to the cause of surgery) and its duration and frequency, pain due to other causes (either acute or chronic, not related to the cause of surgery, but nonetheless frequent), previous surgeries, menopause, diagnosis/indication for hysterectomy and disease onset, as well as the use of psychotropic drugs (anxiolytics and antidepressants).
- The Brief Pain Inventory–Short Form (BPI-SF)[16] was used with patients presenting presurgical pain. It measured the following: pain intensity on an 11-point numerical rating scale (NRS; 0 represents "no pain" and 10 "the worst pain imaginable"); analgesic intake; perception of analgesic relief; pain interference with daily life (general activity, mood, walking, work, relations with others, sleep, and enjoyment of life); and pain location in the body. Higher scores represent higher levels of pain interference. In this study, the internal consistency reliability[18] for the pain interference subscale scores was very high (T1, $\alpha = .92$; T3, $\alpha = .90$).

(2) Psychological Factors
- The Hospital Anxiety and Depression Scale (HADS)[90] was used to measure anxiety (HADS-A)
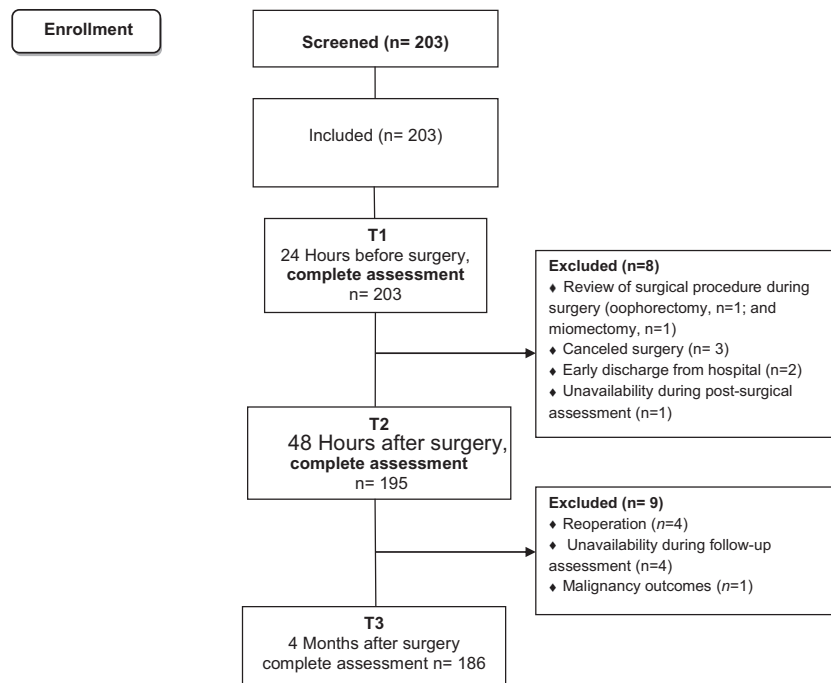
Figure 1. Flowchart (screening, inclusion, and assessment at all data points).

and depression (HADS-B). Each subscale comprises 7 items, with a subscale score ranging from 0 to 21, resulting from the sum of each item on a Likert scale ranging from 0 to 3. Higher scores represent higher levels of anxiety and depression. In the current sample, internal consistency reliability[18] was adequate for both anxiety (T1: α = .78; T2: α = .81; T3: α = .88) and depression (T1: α = .80; T3: α = .85).

- The Revised Illness Perception Questionnaire (IPQ-R)[58] was used to assess patient beliefs about the underlying condition that led to surgery, analyzing distinct dimensions of illness perceptions: "timeline acute/chronic" (eg, "My illness will last for a long time"; α = .78); "timeline cyclical" (eg, "My symptoms come and go in cycles"; α = .75); "consequences" (eg, "The disease underlying surgery has major consequences on my life"; α = .55); "personal control" (eg, "I have the power to influence my illness"; α = .54); "treatment control" (eg, "Surgery can control my illness"; α = .76); "illness coherence" (eg, "My illness is a mystery for me"; α = .78); "emotional illness representation" (eg, "When I think about my illness I get upset"; α = .87). With the exception of "consequences" and "personal control" subscales, with low internal consistency (.55 and .54, respectively), the remaining subscales presented adequate properties. In this study, and with the aim of reducing participant burden, a psychometrically shortened version[80] was used with each of the 7 subscales composed by 3 items each. To generate each total subscale score, the mean response was computed. Hence, each subscale is rated on a scale of 1 to 5, in which high scores reveal less adaptive illness perceptions results, with the exception of personal and treatment control subscales, which score inversely.

- The Surgical Fear Questionnaire (SFQ)[65] was used to assess specific surgical fears through 10 items aggregated in 2 subscales, "fear of immediate consequences of surgery" (6 items) and "fear of long-term consequences of surgery" (4 items). Each item score ranges from 0 to 10; to calculate each total subscale score, the sum of the item scores was divided by the number of items. Thus, each subscale is rated on a scale of 0 to 10, with higher values reflecting higher levels of fear. In the present study, internal consistency[18] was .77 for fear of immediate consequences of surgery and .62 for fear of long-term consequences of surgery.

- The Coping Strategies Questionnaire–Revised Form (CSQ-R)[74] was used to assess 6 coping strategies with pain: "distraction/diverting attention" (α = .77); "praying and hoping" (α = .87); "ignoring pain sensations" (α = .92); "reinterpreting pain sensations" (α = .74); "pain coping self-statements" (α = .71); and "pain catastrophizing" (α = .87). During pilot testing several subjects were confused by the usual 7-point Likert-type scale; therefore, items were presented on a 5-point adjective rating scale (1 = never, 2 = almost never, 3 = sometimes, 4 = almost always, and 5 = always).[65,86] To generate the total subscale score, the sum of the item scores was divided by the number of items. Subscale scores vary between 1 and 5, with higher scores indicating greater use of the specific coping strategy (either adaptive or nonadaptive).

Postsurgical Assessment–48 Hours After Surgery

Forty-eight hours after surgery (T2), women were assessed in a face-to-face interview.

(1) Acute Postsurgical Pain Measurement

Women were asked to rate the intensity of their worst and average pain levels within the first 48 hours after surgery, as well as to identify pain location and perception of analgesics relief (through the BPI-SF questionnaire described above).

Postsurgical pain frequency assessment was performed using the frequency scale of the McGill Pain Questionnaire.[56] Women could define their pain as constant (continuous, steady), intermittent (periodic, rhythmic), or brief (momentary, transient). This specific subscale was used at T2 given that the characterization of a pain that is confined to a period of 48 hours cannot be described in terms of days, weeks, or months, as was done for the assessment of presurgical pain at T1 and of PPSP at T3.

(2) Clinical and Psychological Postsurgical Measures

The use of psychotropic drugs (anxiolytics and antidepressants) during hospital stay was detailed from hospital records. All patients were assigned to a standardized analgesia protocol for 48 hours. This protocol was determined and supervised by the Acute Pain Service and established prior to transferring the patient to the infirmary. Delivery of the analgesic protocol was either epidural or intravenous (IV). The standardized epidural protocols were a) a continuous epidural infusion (delivered infusion balloon) with ropivacaine (.1%) and fentanyl (3 μg/mL); or b) administration of an epidural morphine bolus (2–3 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 (NSAIDs; 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 IV 8/8 hours). In cases of high acute postsurgical pain levels (NRS >3), rescue analgesics were prescribed beyond the standardized analgesic protocol. Due to the great variability in analgesics' protocol and dosages, no attempt was made to determine total equianalgesic medication dosages. It was rather recorded whether rescue analgesics were given to patients or not. Clinical data were obtained from patient medical records. Furthermore, women were assessed on postsurgical anxiety symptoms through the HADS anxiety subscale.

Postsurgical Assessment–4 Months After Surgery

PPSP was defined as pain presence (NRS >0) at 4 months, T3. During the telephone interview at T3 the first question asked was "Do you still have any pain that you could relate to the surgical procedure?" This is an adaptation of the BPI-SF first question on pain prospection. If women answered no, those women were classed as cases without PPSP. This meant that the researcher would then only ask HADS questions and questions on specific clinical variables (see below for full details). If women answered yes, then they were considered PPSP cases and would answer all questions posed to

those without PPSP plus the pain questionnaires BPI-SF[16] and Neuropathic Pain Questionnaire (DN-4).[5,6]

More explicitly, 4 months after surgery (T3), the following measures were assessed with all women, regardless of pain presence or absence, in a standardized telephone interview:

- Clinical variables: use of psychotropic drugs (anxiolytics and antidepressants); menopause status (induced by surgery due to simultaneous performance of oophorectomy) and hormonal replacement therapy (HRT).
- HADS[90]

The following measures were administered only to patients who reported having pain 4 months postsurgery.

- BPI-SF[16]: as described above.
- Pain description: pain frequency was described, similarly to T1, as constant, daily, several times a week, several times a month, during sexual intercourse, by touch or lifting weight.
- DN-4[5,6]: previous research described PPSP as a potential neuropathic pain.[11,34,71] This instrument evaluates pain characteristics/quality through 10 items. Seven of them refer to specific pain sensory descriptors, such as burning, pinpricking, or numbness, and patients answered if their pain had those characteristics through a dichotomous format (yes or no). The last 3 items result from the sensory examination of patients performed by a clinician. For the purposes of this study, only the first 7 items were included (our sample reliability, α = .61).[6] In order to classify the number of patients who might have a potential neuropathic pain condition, a total score was calculated, based on the sum of the number of positive answers to the 7 pain descriptors. This was performed according to Bouhassira et al guidelines (2008),[6] wherein a score of 1 was given to each positive item and a score of 0 to each negative item. The total score was calculated as the sum of the 7 items, and women with a total score $\geq$3 were considered to have neuropathic pain characteristics.

Surgical Procedures and Anesthetic Techniques

Clinical data related to the surgery and anesthesia was retrieved from medical records. From the 186 women who underwent surgery, 135 were submitted to total abdominal hysterectomy, 34 to vaginal hysterectomy, 11 to total laparoscopic hysterectomy, and 6 to laparoscopically assisted vaginal hysterectomy. In abdominal hysterectomies a Pfannenstiel incision (n = 114) was usually the first choice, with a vertical infra-umbilical incision (n = 21) being performed only in cases of existence of a previous vertical surgical scar. Concomitant procedures, such as oophorectomy, ovarian cystectomy, salpingectomy, cystoscopy, or vaginal repair, were also performed in a few patients. We have controlled in all predictive statistical analyses for oophorectomies because of its consequences in terms of the immediate occurrence of early menopause and the eventual intake of HRT. Therefore, we have distinguished women who have entered

menopause because of surgery (simultaneous performance of oophorectomy) from those who did not and kept their previous menopause status. Likewise, HRT consumption was recorded. For all women, uterus weight and height were also recorded. The type of anesthesia was classified as general (n = 53), locoregional (n = 24), or combined (general + locoregional; n = 109) and ASA score (physical status classification of the American Society of Anesthesiologists) was recorded, including cases of ASA grade I (n = 54), II (n = 118), and III (n = 14). Grade I is related to healthy patients, grade II describes mild systemic disease with no functional limitation, and grade III means that severe systemic disease is present with definite functional limitation.[88]

Statistical Analyses

Data were analyzed using the Statistical Package for the Social Sciences (SPSS version 18.0; SPSS Inc, Chicago, IL). Internal consistency of responses to the questionnaires was assessed using Cronbach's alpha.[18] Distribution of predictive data differed significantly from normality assumptions. Thus, continuous variables are presented as median and range, and categorical data are presented as numbers and percentages. The primary outcome variable in this study is the report of PPSP, defined as pain at the 4-month follow-up (yes [presence] or no [absence]). Mann-Whitney test or chi-square tests (χ^2) were performed to compare sociodemographic, clinical, and psychological measures in patients with and without pain 4 months after surgery. Sequential logistic regression analyses were conducted to determine risk factors for PPSP. The sociodemographic, clinical, and psychological variables selected for the regression analysis were those that were found to distinguish between the groups of women with and without pain 4 months after hysterectomy ($P < .05$). Additionally, univariate regression analyses, along with findings of previous studies on acute and persistent (or chronic) pain after different surgical procedures,[26,30,68,70] assisted in the final selection for the logistic sequential regression models. A basic model, embracing sociodemographic and clinical factors, is presented, either alone or as the first step of the subsequent models (4 models). This basic first model tested the predictive role of 4 variables that distinguished the groups in univariate analysis: age, previous surgical pain, pain due to other causes, and type of hysterectomy. The remaining 4 models focused on the role of presurgical predictors (3 models) and on the role of acute postsurgical risk factors (1 model) for PPSP development. Regarding the potential psychological presurgical predictors, 3 models were performed. For all these models, the first step controlled for demographic and clinical variables, while in the next steps the psychological factors that distinguished the groups in univariate analyses were included. One model focused on emotional variables (presurgical anxiety and fear), another tested illness perceptions (cyclical duration, consequences, and emotional illness representation of the condition that led to surgery), and another centered on coping variables (pain catastrophizing). To control for the influence of multicollinearity, the variance inflation factor (VIF) for every independent variable was calculated, being included only if VIF < 2.

Results

Incidence, Characteristics, and Perceived Impact of Pain 4 Months After Hysterectomy

Of the 186 assessed women, 78 reported no pain (NRS = 0) at follow-up and an additional 15 women complained about discomfort, such as numbness or itch, but stated that they did not perceive this as pain. These 2 subgroups of women, making up a total of 93 women, were thus considered as not presenting PPSP. From the remaining 93 women who reported some level of pain the most common locations were the pelvic region (52.7%) and the abdominal scar (49.5%) (Table 1). Some women had pain in more than 1 location. Table 1 demonstrates that of the 93 patients reporting pain 4 months after surgery, 48 perceived it on a daily basis, and 18 several times a week. Ten women reported pain during sexual intercourse and 6 felt pain only when touching the surgical scar. Worst pain intensity was 4 and average pain intensity was 3 on the 0 to 10 NRS. From the 93 women with PPSP, 19 did not identify their pain via any of the DN-4 descriptors, 26 reported 1 descriptor, and 14 women 2 descriptors. Thus, following the cut-off point of ≥3, 59 women (63.4%) did not show any pain with neuropathic features (DN-4 <3), whereas 34 women (36.6%) presented pain with neuropathic characteristics (DN-4 ≥3). Twenty women chose 3 descriptors, 11 women 4, 1 woman 5, 1 woman 6, and 1 woman all 7; the median was 2.

Although 93 women reported PPSP at follow-up, only 16 took analgesics regularly to cope with pain perception, namely paracetamol (16.2%), NSAIDs (13.2%), and antispasmodic (4.4%). Almost half of those feeling pain (44%) reported pain interference in a variety of domains, the most common being mood (73.2%); enjoyment of life (65.9%); general activity (63.4%); normal work (61.0%); and walking ability (53.7%). Table 2 compares women who reported PPSP with women who did not, showing that 54 women entered early menopause as a result of oophorectomy procedures conducted at the same time as the hysterectomy. There were significant differences between women who developed PPSP and those who did not, with the former entering menopause more often due to concomitant oophorectomy procedures. Among those 54 women who entered early menopause, only 24 were taking HRT, although this factor did not show any significant difference between the distinct pain groups. Furthermore, 4 months after hysterectomy, women with PPSP presented more symptoms related to anxiety ($P < .001$) and depression ($P = .001$), although with no differences in psychotropic use.

Table 1. Characteristics and Impact of Pain 4 Months After Hysterectomy (N = 93)

PAIN 4 MONTHS AFTER HYSTERECTOMY – T3	N (%)	MEDIAN	RANGE
Pain report–PPSP*	Yes: 93 (50.0%)		
Location† (can report 1 or more)			
Pelvic region	49 (52.7%)		
Abdominal scar	46 (49.5%)		
Vagina	22 (23.7%)		
Lower back	5 (.05%)		
Frequency			
Daily	48 (51.6%)		
Several times week	18 (19.4%)		
Several times month	11 (11.9%)		
During sexual intercourse	10 (10.8%)		
By touch	6 (6.5%)		
Intensity† (NRS 0–10)			
Worst level		4	.5–10
Average level		3	.5–6
DN-4 total score (total no. of descriptors)		2	0–7
<3	59 (63.4%)		
≥3	34 (36.6%)		
Analgesic consumption†	16 (17.2%)		
Paracetamol	11 (16.2%)		
NSAIDs	9 (13.2%)		
Antispasmodic	3 (4.4%)		

NOTE. Continuous variables are presented as median (range); categorical variables are presented as n (%); T3, 4 months after surgery.
*Women reporting PPSP.
†Items from BPI-SF.

Presurgical (T1) Risk Factors for PPSP 4 Months Following Hysterectomy

Before surgery, women presenting PPSP were younger ($P = .014$) and more likely to be premenopausal ($P = .009$) (Table 2). Groups did not differ in any further sociodemographic measures. Moreover, both groups were similar concerning clinical issues such as surgical disease onset, body mass index, previous surgical procedures, or presurgical psychotropic use. Women with PPSP more often reported presurgical pain ($P = .003$), presenting higher levels of presurgical pain related either to the condition underlying the need for surgery ($P < .001$) or to other causes ($P = .021$), and they were also more likely to report higher total pain interference ($P = .036$) (see Table 2). Furthermore, women with PPSP presented, before surgery, higher anxiety ($P < .001$) and fears associated with the "immediate consequences of surgery" ($P = .007$), worst cognitions associated with the surgical illness ("Cyclical duration": $P = .040$; "Consequences": $P = .008$; "Emotional illness representation": $P < .001$) and higher levels of pain catastrophizing ($P < .001$) (Table 2).

In order to identify the presurgical predictors of PPSP development 4 months after hysterectomy, a set of sequential logistic regression models was conducted (Table 3). The first, most basic model (Model 1) contains 4 variables that have been consistently found to predict PPSP in previous research and that were associated with PPSP in univariate analysis: age, previous surgical pain, pain due to other causes, and type of hysterectomy (see Table 2). Presurgical menopausal status (collinearity with age), type of surgical incision (collinearity with type of hysterectomy), and presurgical pain interference (collinearity with previous surgical pain) as further candidate variables showed considerable overlap to other predictors and were excluded from Model 1 due to multicollinearity (VIFs >2). Model 1 showed that younger women (odds ratio [OR], .945; 95% confidence interval [CI], .907–.985), those who had more pain due to other causes aside from surgical illness (OR, 3.035; 95% CI, 1.499–6.146), and those who underwent open abdominal hysterectomy (OR, 3.233; 95% CI, 1.454–7.187) had a higher risk of developing PPSP; previous surgical pain did not contribute to the prediction of PPSP (see Table 3).

In order to further explore the role of presurgical psychological factors in PPSP development, over and above established demographic and clinical predictors, 3 alternative models were tested adding blocks of variables (the ones that differed between groups at univariate analyses) and measuring emotional distress (Model 2a), illness perceptions (Model 2b), and coping strategies (Model 2c) to the demographic and clinical variables in Model 1 (see Table 3). When adding emotional distress variables (Model 2a), presurgical anxiety emerged as the significant predictor of PPSP development (OR, 1.116; 95% CI, 1.014–1.228), whereas fear of surgery did not and age no longer added to the prediction. In the illness perceptions model (Model 2b; Table 3), illness perception variables were added to the second step, and the presurgical emotional illness representation of surgical disease (emotions in response to the illness underlying hysterectomy) emerged as a significant PPSP predictor (OR, 1.732; 95% CI, 1.201–2.500). Finally, Model 2c (adding coping strategies) shows that presurgical pain catastrophizing contributes to the prediction of PPSP over and above Model 1 variables (OR, 1.753; 95% CI, 1.171–2.624).

The 3 psychological variables found to be predictive of PPSP in models 2a–c were substantially correlated; anxiety correlated with pain catastrophizing (rho = .56) and with emotional illness representations (rho = .49). Emotional illness representations and pain catastrophizing correlated (rho = .46), suggesting that the underlying processes might be interrelated. The potential shared variance among the psychological variables, as well as the number of predictors, contributed to the decision to test the contribution of each of the psychological putative predictors in separate predictive equations. Nevertheless, for the purposes of prediction, a regression analysis regressing PPSP onto all those demographic, clinical, and psychological predictors found to add significantly to the predictions (see Table 3) was conducted. From Model 1 we have included the 3 predictors that emerged as significant: age, type of hysterectomy, and pain due to other causes. From Model 2a we retained presurgical anxiety; from Model 2b, emotional illness representation; and from Model 2c, pain catastrophizing. All of the 3 predictors on the initial step (age, type of hysterectomy, and pain due to other causes) emerged as significant predictors of PPSP. Regarding the

Table 2. Differences Between Women With and Without Pain (T3) on Sociodemographic, Clinical, and Psychological Measures Determined at T1, T2, and T3

MEASURES	TOTAL (N = 186)	NO. PPSP (N = 93)	PPSP (N = 93)	P
Women baseline characteristics—T1				
Sociodemographic: Age (years)	49 (35–76)	50 (37–76)	48 (35–68)	.014
Clinical-presurgical pain indicators				
Presurgical pain (yes)	112 (60.2%)	46 (49.5%)	66 (71.0%)	.003
Intensity* (worst level)	2.5 (0–10)	1 (0–10)	5 (0–10)	<.001
Pain total Interference* (0–10)	0 (0–7.6)	0 (0–4.7)	.7 (0–7.6)	.036
Pain due to other causes (yes)†	121 (65.1%)	53 (57.0%)	68 (73.1%)	.021
Psychological variables				
HADS: Anxiety	7 (0–19)	6 (0–15)	8 (0–19)	<.001
HADS: Depression	1 (0–14)	1 (0–12)	1 (0–14)	ns
SFQ: Immediate consequences	2.83 (0–9)	2.33 (0–9)	3.08 (0–7.7)	.007
SFQ: Long-term consequences	.75 (0–8.8)	.50 (0–8.8)	1.0 (0–6.5)	ns
IPQ-R: Timeline acute/chronic	2 (1–4)	2 (1–4)	2 (1–3.7)	ns
IPQ-R: Timeline cyclical	2.3 (1–4.7)	2 (1–4.3)	2.7 (1–4.7)	.04
IPQ-R: Consequences	2 (1–4.3)	1.67 (1–4.3)	2 (1–4.3)	.008
IPQ-R: Personal control	2 (1–4.3)	2 (1–4.3)	2 (1.3–4)	ns
IPQ-R: Treatment control	4 (3–5)	4 (3–5)	4 (3.3–5)	ns
IPQ-R: Illness coherence	3.3 (1–4.7)	3.3 (1–4.7)	3.3 (1.3–4.7)	ns
IPQ-R: Emotional illness representation	2.67 (1–5)	2 (1–5)	3.3 (1–5)	<.001
CSQ-R: Pain catastrophizing	1.5 (1–5)	1.3 (1–4.3)	1.7 (1–5)	<.001
CSQ-R: Ignoring pain	2.4 (1–5)	2.6 (1–5)	2.2 (1–5)	ns
CSQ-R: Self-statements with pain	4 (1.5–5)	4.3 (1.5–5)	4 (1.8–5)	ns
CSQ-R: Reinterpret. pain sensations	1.5 (1–5)	1.5 (1–4.8)	1.5 (1–5)	ns
CSQ-R: Praying and hoping	3.7 (1–5)	3.3 (1–5)	3.7 (1–5)	ns
CSQ-R: Distraction/diverting attention	1.8 (1–5)	1.6 (1–4.4)	1.8 (1–5)	ns
Postsurgical data 48 hours after surgery—T2				
Type hyst:‡ open abdominal	135 (72.6%)	57 (61.3%)	78 (83.9%)	.001
Abdom. incis.§ Pfannenstiel	114 (61.3%)	44 (47.3%)	70 (75.3%)	<.001
Acute postsurgical pain intensity*	5 (0–10)	4 (0–10)	5 (1–10)	<.001
Pain frequency:¶ constant	58 (31.9%)	20 (19.8%)	38 (46.9%)	<.001
HADS: Anxiety	2 (0–19)	1 (0–13)	3 (0–19)	<.001
Postsurgical data 4 months after surgery—T3				
Menopause due to surgery	54 (29.0%)	19 (20.4%)	35 (37.6%)	.01
HRT# (yes)	24 (44.4%)	6 (31.6%)	18 (51.4%)	ns
HADS: Anxiety	4 (0–20)	2 (0–12)	6 (0–20)	<.001
HADS: Depression	0 (0–16)	0 (0–9)	1 (0–16)	.001

NOTE. Continuous variables are presented as median (range); categorical variables are presented as n (%); T1, 24 hours before surgery; T2, 48 hours after surgery; T3, 4 months after surgery.
*Items from BPI-SF.
†Other previous pain states (either acute or chronic, not related to the cause of surgery, but nonetheless frequent).
‡Type of hysterectomy: n (%) of open abdominal hysterectomies versus abdominal laparoscopic, vaginal, and vaginal assisted laparoscopic.
§Abdominal incision: n (%) of Pfannenstiel incisions versus infraumbilical vertical incision and laparoscopies.
¶Pain frequency: constant pain versus intermittent or brief pain, assessed via frequency subscale of McGill Pain Questionnaire.
#HRT due to menopause occurrence because of surgery (hysterectomy + bilateral oophorectomy).

psychological variables included (in a same step), only emotional illness representation of the condition that led to surgery (OR, 1.673; 95% CI, 1.108–2.525) emerged as the single psychological predictor of PPSP, with presurgical anxiety and catastrophizing not yielding significant results when together with this variable in the same regression.

Postsurgical (T2) Risk Factors for PPSP 4 Months Following Hysterectomy

Forty-eight hours after surgery, abdominal hysterectomy (P = .001) and Pfannenstiel incision (P < .001) were more significantly associated with the occurrence of PPSP (Table 2). The groups did not show any difference

in other clinical parameters such as uterus weight and height, type of anesthesia, type of analgesia, length of stay, or consumption of psychotropic. Women who presented PPSP at T3 revealed a heightened acute pain experience 48 hours after surgery (P < .001), having pain more frequently (P < .001). Moreover, after surgery these women were also more anxious (P < .001) than those without pain 4 months after hysterectomy (Table 2).

Table 4 shows a similar sequential logistic regression model to the one in Table 3 testing the additional predictive utility of postsurgical variables (T2) for PPSP over and above the same demographic and clinical variables used for Model 1 in Table 3. At step 2, acute postsurgical pain intensity and frequency were included. Interestingly, only pain frequency yielded significant results, with

Table 3. Sequential Logistic Regression Analysis of Persistent Postsurgical Pain 4 Months Following Hysterectomy on Demographic, Clinical, and Psychological Measures at Baseline

MODELS	WALD	ODDS RATIO (CI)	P
Model 1—Demographic and clinical predictors			
Age*	7.253	.945 (.907–.985)	.007
Type of hysterectomy†	8.286	3.233 (1.454–7.187)	.004
Presurgical pain‡	.930	1.416 (.699–2.869)	ns
Pain due to other causes‡	9.514	3.035 (1.499–6.146)	.002
Model 2a—Emotional distress (Final Model)			
Age*	2.672	.966 (.928–1.007)	ns
Type of hysterectomy†	6.489	2.774 (1.265–6.081)	.011
Previous presurgical pain‡	1.722	1.629 (.786–3.377)	ns
Pain due to other causes (yes)‡	5.314	2.302 (1.133–4.679)	.021
Presurgical anxiety§	5.033	1.116 (1.014–1.228)	.025
Presurgical fear¶	.434	1.064 (.885–1.279)	ns
Model 2b—Illness perceptions (Final Model)			
Age*	4.934	.950 (.909–.994)	.026
Type of hysterectomy†	8.343	3.217 (1.456–7.108)	.004
Previous presurgical pain‡	2.570	1.944 (.862–4.384)	ns
Pain due to other causes (yes)‡	7.372	2.756 (1.326–5.729)	.007
Timeline cyclical#	3.173	.675 (.438–1.040)	ns
Consequences#	1.178	1.323 (.798–2.194)	ns
Emotional illness representation#	8.631	1.732 (1.201–2.500)	.003
Model 2c—Coping strategies (Final Model)			
Age*	4.872	.956 (.919–.995)	.027
Type of hysterectomy†	4.654	2.346 (1.081–5.091)	.031
Previous presurgical pain‡	1.385	1.525 (.755–3.082)	ns
Pain due to other causes (yes)‡	4.144	2.063 (1.027–4.144)	.042
Pain catastrophizing**	7.424	1.753 (1.171–2.624)	.006

Abbreviation: ns, not significant.
MODELS
Model 1: after removing 3 outliers, this model correctly predicted 66.8% of all patients; $\chi^2(4) = 35,136$; $P < .001$; Nagelkerke $R^2 = .233$.
Model 2a: after removing 2 outliers, this model correctly predicted 66.8% of all patients; $\chi^2(6) = 40,230$; $P < .001$; Nagelkerke $R^2 = .262$.
Model 2b: after removing 2 outliers, this model correctly predicted 70.1% of all patients; $\chi^2(7) = 44,550$; $P < .001$; Nagelkerke $R^2 = .287$.
Model 2c: after removing 1 outlier, this model correctly predicted 68.1% of all patients; $\chi^2(5) = 37,185$; $P < .001$; Nagelkerke $R^2 = .243$.
*Continuous variable, in years.
†Dichotomous variable: 0 = abdominal laparoscopic, vaginal, and vaginal assisted laparoscopic; 1 = open abdominal hysterectomies.
‡Dichotomous variable: 0 = No, 1 = Yes.
§Continuous variable, HADS-A.
¶Continuous variable, SFQ, fear of immediate consequences of surgery subscale.
#Continuous variable, IPQ-R, timeline cyclical, consequences and emotional representation subscales.
**Continuous variable, CSQ-R, pain catastrophizing subscale.

constant acute postsurgical pain emerging as a predictor (OR, 2.251; 95% CI, 1.043–4.861) of later development of persistent pain. Furthermore, postsurgical anxiety was added to the model in step 3, emerging as a significant predictor (OR, 1.155; 95% CI, 1.015–1.315). However, after this addition, in the final model, pain frequency ceased to be significant, although predictors of step 1 remained significant. Correlation between postsurgical and presurgical anxiety was lower (rho = .43) than the correlations observed between different psychological distress variables assessed at T1.

Discussion

This is the first study to identify the joint role of demographic, clinical, and psychological risk factors for persistent pain experience 4 months after hysterectomy due to benign disorders. Among the assessed risk factors, age, pain due to other causes, and type of hysterectomy were the key demographic and clinical predictors of PPSP development. Regarding baseline presurgical psychological factors, anxiety, emotional illness representations, and dysfunctional pain coping through catastrophizing were found to be additional risk factors for PPSP. When testing all the psychological predictors at once, the single best predictor was emotional illness representation. Postsurgical anxiety added to the prediction. Results of this study improve knowledge on PPSP and increase potential intervention targets for healthcare professionals.

Pain 4 Months After Hysterectomy

Half of women reported pain 4 months after hysterectomy, and half of these complained of daily pain. Furthermore, those with pain presented more anxious and depressive symptomatology. Another hysterectomy study found lower prevalence rates of PPSP (eg, 16.7%) 4 months after.[8] A key distinction between the present and the previous study is the way we define persistent pain: any kind of pain linked to the surgical procedure, regardless of its location, intensity, interference, or concomitant analgesic consumption.[70] As it is not well understood why some patients are totally pain-free shortly after surgery and others suffer from ongoing postsurgical pain,[41] and given that a mild pain problem can impact daily life, we opted to use the criteria proposed by Poleshuck et al.[70]

Predictors of Pain 4 Months After Hysterectomy

Demographic and Clinical Baseline Predictors

In line with previous evidence, type of hysterectomy and pain due to other causes were found to predict PPSP. Abdominal hysterectomies have been associated with higher acute postsurgical pain than vaginal hysterectomies,[32] as open abdominal surgeries are among the most painful surgical procedures.[15,35] Vaginal route[42,78] or laparoscopic[14,24,52] approaches to hysterectomy should be considered when possible.

The existence of pain due to other causes emerged as a predictor of PPSP, although presurgical pain (related to surgery) was not significant. Presurgical pain was not the only reason for surgery: 40% of women did not present pain symptoms related to the scheduled surgery. These results are consistent with those of other

Table 4. Sequential Logistic Regression Analysis of Persistent Postsurgical Pain 4 Months Following Hysterectomy on Demographic and Clinical Baseline Measures, and Postsurgical Pain and Anxiety 48 Hours After Surgery

MODELS	WALD	ODDS RATIO (CI)	P
Step 1			
Age*	6.732	.948 (.911–.987)	.009
Type of hysterectomy†	7.447	2.974 (1.360–6.507)	.006
Previous presurgical pain‡	1.831	1.620 (.805–3.259)	ns
Pain due to other causes (yes)‡	9.135	2.948 (1.462–5.942)	.003
Step 2			
Postsurgical pain intensity§	1.815	1.090 (.962–1.236)	ns
Postsurgical pain frequency¶	4.273	2.251 (1.043–4.861)	.039
Step 3 (Final Model)			
Age*	3.974	.957 (.917–.999)	.046
Type of hysterectomy†	5.571	2.670 (1.181–6.037)	.018
Previous presurgical pain‡	1.663	1.633 (.775–3.439)	ns
Pain due to other causes (yes)‡	4.090	2.147 (1.024–4.503)	.043
Postsurgical pain intensity§	.162	1.029 (.897–1.179)	ns
Postsurgical pain frequency¶	2.024	1.793 (.802–4.010)	ns
Postsurgical anxiety#	4.789	1.155 (1.015–1.315)	.029

Abbreviation: ns, not significant.

NOTE. After removing 4 outliers, this final model correctly predicted 65.9% of all patients; $\chi^2(7) = 49,029$; $P < .001$; Nagelkerke $R^2 = .315$.

*Continuous variable, in years.

†Dichotomous variable: 0 = abdominal laparoscopic, vaginal, and vaginal assisted laparoscopic; 1 = open abdominal hysterectomies.

‡Dichotomous variable: 0 = No, 1 = Yes.

§Continuous variable, NRS 0–10 from BPI-SF.

¶Dichotomous variable: 0 = intermittent or brief pain, 1 = constant pain, frequency subscale of McGill Pain Questionnaire.

#Continuous variable, HADS-A.

studies[8,9,50,89] and suggest that prolonged pain stimulation can exacerbate the nociceptive system through mechanisms of peripheral and central sensitization of nociceptors and central nervous system neurons, respectively.[39] It is possible that this may contribute to an association between the existence of pain due to other causes and PPSP.

Although not so consistently, age was also found to be a risk factor for PPSP, with younger women being more likely to report PPSP, which is consistent with results from other types of surgery.[4,11,13,21,31,36,40,71] The protective effect of increased age has been related to a reduction in peripheral nociceptive function.[64,84]

The Role of Psychological Predictors

The finding that psychological measures related to negative affect were predictive of PPSP over and above age and clinical variables adds to our understanding.

While previous research has identified presurgical anxiety as a risk factor for acute postsurgical pain, few studies have provided evidence for its role in PPSP development.[7,23,27] Forty-eight hours after surgery, anxiety was, again, predictive of PPSP. Surprisingly, never before was anxiety after surgery studied as a potential predictor for PPSP. It can therefore be assumed that anxiety before and after surgery seems to affect PPSP.

Contrary to expectations, the present study did not find acute postsurgical pain intensity as a predictor,[3,59,63] but rather acute postsurgical pain frequency. This is the first time this effect has been shown. While we found that postsurgical pain frequency, rather than intensity, as suggested by previous research,[59,60,62] added to the prediction over age and clinical variables, this relationship was attenuated to insignificance when postsurgical anxiety was entered (see Table 4).

To our knowledge, this was the first study to test illness perceptions as potential risk factors for postsurgical pain. We found that emotional illness representations, eg, the affective response to the condition addressed by the hysterectomy, predicted PPSP. In the current study the emotional illness representation of the health threat emerged as a significant predictor, which means that the specific emotional response to the illness, such as feeling depressed, angry, or upset, appears to influence pain outcomes. This scale does not constitute a simple indicator of patients' general mood, but provides an evaluation of the emotional responses triggered by illness, regardless of its actual severity.[58] In patients with osteoarthritis, those reporting more negative emotional illness representations experienced more limitation in daily activities than explained by objective limitations diagnosed by radiographs.[4] When testing for the contribution of each of the psychological predictors together, emotional illness representation was the only variable that remained significant.

Pain catastrophizing has been found to be a reliable predictor of acute postsurgical pain,[26,68] and there is some emerging evidence for its role as risk factor for PPSP, just like in this study.[22,73,82]

The predictive models seem to demonstrate that negative emotions as well as maladaptive coping skills (pain catastrophizing) can influence the development of PPSP.

Limitations of the Study

A potential limitation is the absence of a physical examination of women reporting pain at T3. This study focused on pain as experienced by women after hysterectomy. Future research could also test for inflammatory or neuropathic elements and analyze nerve injury to provide a more comprehensive model of factors contributing to pain. It would also have been important to measure the length of incision in women who had an open abdominal hysterectomy, to clarify and understand this issue as a potential risk factor.[47,55,69,79,85] The lack of a physical examination also prevented the administration of the latter 3 items of DN-4[5] questionnaire, but the use of the self-reported 7-item questionnaire is acknowledged as a valid procedure.[6]

Psychological measures, with the exception of anxiety and depression at T3, were assessed prospectively only before the scheduled hysterectomy. We might argue that they should be reassessed after surgery, during T2, given the likely impact of surgery on these variables, with arguments for and against. However, at T2 the goal was to reduce questionnaire burden by keeping

the number of variables assessed to a minimum and assessing those likely to change 48 hours postsurgery. At T3 the aim was to collect data on our outcome variable (PPSP) using T1 and T2 variables as predictors. Moreover, T3 measures were obtained through a telephone interview.

Another possible limitation of this study is related to the clarification of PPSP etiology. Understanding to what extent chronic or persistent pain after hysterectomy results from a new pain or merely reflects a continuation of the previous pain that led to surgery[10,50] is fundamental. In the predictive analysis conducted in this study, presurgical pain was not a significant predictor, which may reflect a major role of new pain.

Given the aims of this clinical observational study, we used presurgical pain scores (linked not only to presurgical pain, but also to pain due to other causes not related to the diagnosis that led to surgery) as a clinical measure of pain. We acknowledge the potential importance of assessing interindividual differences in pain sensitivity through the performance of experimental pain sensitivity tests. Future studies can potentially add to our understanding of pain sensitivity in predicting PPSP if experimental sensitivity measures are taken.

Clinical Implications

In terms of presurgical interventions, younger women who come for surgery and are screened with other previous chronic pain states could be offered special care in terms of presurgical intervention. Our results suggest that women should be screened for emotional distress, illness perceptions, and pain coping strategies. For those with high levels of anxiety, pain catastrophizing, and worst emotional illness representation, brief psychological presurgical interventions could be delivered. To deal with anxiety, cognitive behavior therapy interventions (eg, brief relaxation)[12,25,75] could be provided before surgery. Addressing emotional illness representations

might be a more promising strategy as specific beliefs can be more easily modified in brief interventions than broader emotional states such as anxiety. Pain catastrophizing can be targeted before surgery through cognitive pain coping interventions, such as distraction techniques, pain ignoring strategies, and positive coping self-statements.[12,20,25,53,75] After assessment, patients could be assisted by health professionals in learning and applying more effective coping skills and to manage their emotional illness representations.[29]

The surgical procedures should be carefully selected, considering all individual characteristics. Future research should evaluate the potential risk of abdominal hysterectomies, making sure that a more accurate and detailed physical assessment of the patient and of the incision per se is conducted.

After surgery, data from this study indicates that anxiety levels should be monitored and managed. Moreover, special care should be directed to those surgical patients who frequently report pain and are unable to get efficient relief from analgesics.

Psychological interventions, either before or immediately after surgery, could focus on acute postsurgical pain control and management[19,33] in order to further support patients to prevent PPSP development.

In sum, by identifying patients at risk of developing PPSP, more accurate surgical and analgesic individual approaches can be implemented along with appropriate short-term psychological interventions and better postsurgical surveillance.

Acknowledgments

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