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Are Psychological Predictors of Chronic Postsurgical Pain Dependent on the Surgical Model? A Comparison of Total Knee Arthroplasty and Breast Surgery for Cancer

Anne Masselin-Dubois,[*,†] Nadine Attal,[*,†,‡] Dominique Fletcher,[*,†,‡,§] Christian Jayr,[¶] Aline Albi,[¶] Jacques Fermanian,[||] Didier Bouhassira,[*,†,‡] and Sophie Baudic[*,†,‡]

**INSERM U-987, Boulogne-Billancourt, France.*
[†]CHU Ambroise Paré, GH Paris Ile de France Ouest, APHP, Boulogne-Billancourt, France.
[‡]Université Versailles-Saint-Quentin, Versailles, France.
[§]Service d'anesthésie-réanimation chirurgicale, CHU Raymond Poincaré, GH Paris Ile de France Ouest, APHP, Garches, France.
[¶]Service de chirurgie générale, Hôpital René Huguenin-Institut Curie, Saint Cloud, France.
[||]Service de biostatistiques, CHU Necker, APHP, Paris, France.

Abstract: Anxiety, depression, and catastrophizing are generally considered to be predictive of chronic postoperative pain, but this may not be the case after all types of surgery, raising the possibility that the results depend on the surgical model. We assessed the predictive value of these factors for chronic postsurgical pain in 2 different surgical models: total knee arthroplasty for osteoarthritis (89 patients, 65% women, age = 69 ± 9 years, baseline pain intensity = 4.7 ± 2.1) and breast surgery for cancer (100 patients, 100% women, age = 55 ± 12 years, no preoperative pain). Data were collected before surgery, then 2 days and 3 months after surgery. Anxiety, depression, and catastrophizing were measured with the Spielberger State-Trait Anxiety Inventory, Beck Depression Inventory, and Pain Catastrophizing Scale, respectively. Pain was assessed with the Brief Pain Inventory. Neuropathic pain was detected with the DN4 questionnaire. Multivariate logistic regression analyses for the total knee arthroplasty and breast surgery models considered together indicated that the presence of clinically meaningful chronic pain at 3 months (pain intensity ≥3/10) was predicted independently by age (*P* = .04), pain intensity on day 2 (*P* = .009), and state anxiety (*P* = .001). Linear regression models also showed that pain magnification, one of the dimensions of catastrophizing, independently predicted chronic pain intensity (*P* = .04). These results were not affected by the surgical model or by the neuropathic characteristics of the pain. Thus, state anxiety and pain magnification seem to constitute psychological risk factors for chronic postsurgical pain relevant in all surgical models.

***Perspective:** This prospective study performed in patients with total knee arthroplasty or breast surgery for cancer shows that state anxiety, amplification of pain, and acute postoperative pain independently predict postsurgical pain at 3 months and that this does not depend on the surgical model.*

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***Key words:** Postsurgical pain, anxiety, depression, catastrophizing, neuropathic pain, total knee arthroplasty, breast surgery.*

Chronic postsurgical pain is a significant health problem.[24,27] The impact of sociodemographic and physical factors has been largely demonstrated (see[20,24] for reviews) and the role of psychological factors has been evaluated more recently in prospective studies (for reviews, see[19,20,24,27,48]). Anxiety and depression have been evaluated most frequently,[19] but pain cognition, including catastrophizing in particular, is increasingly being considered.[27,48] However, discrepant results have been reported regarding the role of these predictors in chronic postsurgical pain and their relationship. For example, preoperative

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Address reprint requests to Nadine Attal, INSERM U-987 and Centre d'Evaluation et de traitement de la Douleur, Hôpital Ambroise Paré, APHP, 9 avenue Charles de Gaulle, 92100 Boulogne-Billancourt, France. E-mail: nadine.attal@apr.aphp.fr

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anxiety and depression have been found to be predictive of chronic postsurgical pain, particularly after musculoskeletal surgery,[48] but not after other types of surgery (eg, prostatectomy, chest surgery, hysterectomy, herniotomy)[8,14,28] or were not independently associated with pain after breast surgery.[36] Other studies have shown that only early postoperative depression was predictive of chronic pain after spine surgery.[41] Similarly, pain catastrophizing has been found to be predictive of chronic pain after total knee arthroplasty (eg,[11,45]) or spine surgery,[2,10] but not after chest surgery[28] or hysterectomy.[8] Catastrophizing assessed 1 month after limb amputation has even been found to predict a favorable outcome 5 to 12 months later.[16,21] All these studies were performed in single surgical models, making it impossible to determine whether the role of psychological predictors is dependent on the surgical model or similar in various types of surgery, despite the heterogeneity of procedures, age and sex, the presence or absence of preoperative pain, the benignity or malignancy of the lesion, and the distinct quality of postoperative pain.

We addressed this question by comparing the extent to which affect (anxiety, depression) and pain cognition (catastrophizing) were predictive of the prevalence and intensity of chronic postsurgical pain 3 months after the intervention, in 2 different surgical models: total knee arthroplasty (TKA) for osteoarthritis, a benign intervention mostly carried out in elderly people having chronic preoperative pain[45,46]; and breast cancer surgery, mostly in younger women with little or no preoperative pain.[12] We hypothesized that it might be possible to detect predictive affective or cognitive risk factors common to both these surgical models, despite their heterogeneity, which therefore could be considered potentially "invariant" risks for chronic postsurgical pain. These surgical models also induce different types of pain: mostly non-neuropathic pain in the TKA model and neuropathic pain in the breast surgery model. We therefore also assessed the impact of the same predictive variables on pain with neuropathic characteristics (NC) in both models.

Methods

Participants and Procedure

The study sample consisted of 2 groups of patients undergoing TKA or breast cancer surgery, recruited between May 2008 and September 2011. The study was approved by the local ethics committee (Comité de Protection des Personnes Ile-de-France VIII), and all patients were asked to provide informed consent for the study.

TKA patients were recruited from the Raymond Poincaré Hospital (APHP, Garches, France). Eligible patients were women or men aged 18 to 85 years, scheduled for unilateral TKA for osteoarthritis of the knee. Patients were not included if they had conditions other than osteoarthritis necessitating TKA (eg, rheumatoid arthritis, spondylarthropathy), required bilateral TKA, or had undergone previous knee surgery. Surgery was performed in the same surgical ward in each case, by 1 of 3 highly experienced surgeons, in an identical, standardized protocol (median skin incision, paramedial arthrotomy, condylar femoral and tibial components implanted and cemented). The anesthetic procedure was similar for all patients and combined propofol, sufentanil, a muscle relaxant, and sevoflurane. In all patients, postoperative pain was controlled by intravenous morphine patient-controlled analgesia together with intravenous acetaminophen, ketoprofen, and a femoral peripheral nerve block. At follow-up, all the radiographic data confirmed that all implants were well aligned mechanically and that implant placement was satisfactory. There was no evidence of ligament instability, and none of the patients displayed implant displacement at the time of assessment.

The second group of patients consisted of women aged 18 to 85 years recruited from René Huguenin Hospital (Saint Cloud, France) for mastectomy or lumpectomy to treat breast cancer, with axillary lymph node dissection in all cases. The intercostobrachial nerve is more likely to be damaged in these conditions, and this damage may result in chronic neuropathic pain.[36] Surgery was performed in the same surgical ward in each case, by 1 of 5 surgeons, according to an identical procedure. The lumpectomy and mastectomy groups did not differ in terms of the incidence or severity of postsurgical pain, as previously reported,[36] and were therefore analyzed together. Furthermore, the choice of surgeon had no impact on the prevalence or intensity of pain at 3 months (not shown). Women were not included if they had any past surgery of the thoracic or cervicobrachial region, including prior mastectomy or lumpectomy; were scheduled for lumpectomy for a benign tumor, for bilateral mastectomy, or for a second breast surgery procedure during the 3 months of follow-up; had other malignant conditions or evidence of distant metastases (apart from lymph node macrometastases); or had undergone radiotherapy or chemotherapy before surgery. Data for radiotherapy and chemotherapy during the 3 months following surgery were obtained from the patients' medical reports or were directly reported by the patients. The anesthetic procedure was similar for all patients: general anesthesia was induced with propofol, sufentanil, and atracurium or cisatracurium, to facilitate orotracheal intubation. Anesthesia was maintained with nitrous oxide, sevoflurane, or desflurane and boluses of sufentanil, as required. In all patients, postoperative pain was controlled by intravenous acetaminophen.

All the patients in both surgical groups were native French speakers. We did not include patients with clinically significant or unstable psychiatric or somatic conditions (eg, major depression, psychosis, uncontrolled diabetes mellitus or hypertension, neurologic disorders, immune disease, or body mass index >45), cognitive impairment, or past or present substance abuse.

Participants were asked to complete questionnaires about their demographic characteristics, trait anxiety, and catastrophizing 1 month prior to surgery and then were again questioned about their pain status and intensity, state anxiety, and depression the day before surgery in the presence of a certified psychologist (A.M.-D. or S.B.). Because state and trait anxiety do not measure the same dimension of anxiety, they were administered at distinct time points. Another reason for choosing distinct periods of administration before surgery was the fact that we also used other questionnaires and we wished to reduce the length of testing sessions. Patients were questioned again about their postsurgical pain status 2 days after surgery (during their hospital stay) by the anesthesiologist, and then via a postal survey 3, 6, and 12 months after surgery, but the data obtained at 6 and 12 months will be presented separately. The level of missing data was minimized by having the investigators telephone those who did not send their pain evaluation at 3 months.

Measurements

Pre- and Postoperative Pain

Identical questionnaires were used to assess pain in the 2 surgical groups, to ensure that the results obtained were comparable. The Brief Pain Inventory (BPI)[9] was used to assess "average pain intensity" on a numerical scale from 0 (no pain) to 10 (pain as bad as you can imagine) (ie, "please rate your pain by circling the one number that best described your pain on the average") preoperatively and 3 months postoperatively, and "pain right now" on a 0 to 10 numerical scale 48 hours after surgery. Clinically meaningful pain was considered to be present if patients rated their average pain or pain right now as ≥3/10 on the BPI. This cutoff corresponds to at least moderate pain with a potential impact on physical or emotional functioning. The BPI interference score was also used at baseline in patients scheduled for TKA and 3 months after surgery in both groups to measure pain interference with daily activities.[9] This is a 7-item scale measuring the degree to which pain interferes with areas of daily life: general activity, mood, walking, work, relations with others, sleep, and enjoyment with life (0 = do not interfere to 10 = completely interfere). Patients were asked to fill this questionnaire if they had at least minimal pain (≥1/10). For patients without pain, the score for BPI interference was 0.

The 7-item version of the DN4 questionnaire was used to screen for the presence of pain with NC before surgery in patients scheduled for TKA then at 3 months in both groups, with a score ≥3/7 considered indicative of pain with NC with good sensitivity (78%) and specificity (81.2%).[5] It has been used in several prospective epidemiologic surveys to assess the prevalence of pain with NC (eg, see ref[6]).

Emotional Functioning

We assessed emotional functioning before surgery with 2 different tools in both groups. The 13-item Beck Depression Inventory[3] was used to assess the presence and severity of depressive symptoms. For this scale, each item is scored on a 4-point scale (0–3), with higher scores reflecting more severe symptoms (range 0–39, with higher scores indicating greater depression). The Spielberger State Trait Anxiety Inventory was used to assess self-reported anxiety.[43] The state form (20 items) was used to assess the severity of preoperative anxiety, whereas the trait form (20 items) was used to assess the more general anxiety status of the subject (range 20–80, with higher scores indicating greater anxiety).

Cognition and Pain-Related Behavior

The French version of the Pain Catastrophizing Scale (PCS) was used before surgery in both groups to assess catastrophic thinking related to pain.[44] The PCS consists of 13 items describing the thoughts and feelings that individuals may experience when in pain (range 0–52). Factor analysis identified 3 distinct dimensions: magnification, rumination, and helplessness. The PCS has been shown to be highly internally consistent and to be associated with heightened pain and disability in patients with osteoarthritis.[46] Women scheduled for breast interventions completed this questionnaire by referring to past experiences of pain. In these women, the PCS was administered again 2 days after surgery, during the period of acute postoperative pain.

Statistical Methods

Descriptive statistics were used to summarize the demographic and clinical characteristics of the sample. The relationships between study variables before surgery were assessed with the Spearman correlation coefficients (rho). The correlations between presurgical values and the values obtained 3 months after surgery were also assessed with the Spearman rho. Student t-tests for quantitative variables and corrected χ^2 tests for categorical variables were performed to compare the demographic, clinical, and preoperative emotional/cognitive data between patients who did and did not develop chronic pain at 3 months, and between the groups of patients with pain who did and did not develop pain with NC. Wilcoxon signed rank tests were used to compare pain intensity before surgery and 3 months after surgery.

To identify independent factors predictive of the presence of clinically meaningful pain in the total sample of patients (based on a score ≥3/10 on the BPI at 3 months) and to check whether these factors differed between surgical groups (presence or absence of an interaction between each predictive variable and surgery used as a moderator variable), we built the following logistic regression model:

Step A: Selection of independent variables. These included the surgical group (as a categorical variable: TKA, breast), age (as a continuous variable), postoperative pain at 2 days (yes: ≥3/10, no: <3/10), and 3 measurements of affect/cognition (Beck Depression Inventory, Spielberger State Anxiety, PCS score or 1 of its 3 subscores, as continuous variables). These variables were entered in the model if they were found to distinguish between patients with and without pain in univariate analyses in both surgical groups, using a liberal significance level of $P < .20$ in all cases.

Step B: Addition of all the interactions between each independent variable and the moderator variable "surgery."

Similarly, linear regression analyses were conducted for the total sample of patients, to identify independent factors predictive of postsurgical pain intensity (with average pain intensity on the BPI as a continuous variable).

Independent variables were entered in this model if they were found to be correlated with postsurgical pain intensity in univariate analyses in both surgical groups, using a liberal significance level of $P < .20$. These variables were entered in addition to all the interactions between each independent variable and the moderator variable "surgery." Finally, logistic regression analyses were conducted using the same statistical model in the subsample of patients with pain from both surgical groups to identify independent factors predictive of the presence of pain with NC at 3 months (based on a score ≥3/7 on the DN4 questionnaire).

Two regression analyses were calculated for each model: the backward selection included only variables with *P* values < .10 in multivariate analyses, and the full model included all the independent variables proposed for regression analysis and their respective interactions with the surgical model.

Statistical analyses were performed with SAS/STAT 9.1 (SAS Institute, Cary, NC), by an independent statistician. We considered *P* values < .05 to be significant.

Results

Characteristics of the Patients

Fig 1 shows a flow chart outlining the recruitment of patients for this study. In total, we contacted 220 consecutive patients scheduled to undergo TKA at Raymond Poincaré Hospital (Garches) concerning possible participation in this study: 55 declined to participate and 35 were ineligible (prior TKA, TKA for rheumatoid arthritis or spondylarthropathy, significant medical/psychiatric comorbidity, cognitive disorders, or language difficulties). In total, 144 subjects provided informed consent, 55 of whom were subsequently excluded (refusal of the whole testing; cancellation of surgery; or cognitive, language, or visual disorders detected during testing). Overall, 89 patients completed the presurgical assessment; 83 (94%) were assessed on day 2 and 89 were reassessed at 3 months.

In total, 207 consecutive women scheduled for total mastectomy or lumpectomy with lymph node resection at René Huguenin Hospital were asked to participate in the study: 49 declined to participate, and 41 were ineligible (age >85 years, cognitive disorders, preoperative chemotherapy, language difficulties, previous breast surgery, or psychiatric comorbidity). Thus, 120 women provided informed consent, but 20 were subsequently excluded (refusal of testing or cognitive deficits detected during testing). In total, 100 women were assessed before surgery and reassessed at day 2 and at 3 months.

The clinical, demographic, and psychological characteristics of the patients are indicated in Table 1. The TKA sample consisted of 89 patients (65% women), generally elderly or middle-aged (mean age = 68.7 ± 8.9 years), with chronic pain due to osteoarthritis of the knee: 84% had at least moderate pain, pain duration was 13.7 ± 13.3 years (range = 0–53), average pain intensity was 4.7 ± 2.1 (range = 0–9), and interference with pain (on the BPI) was 30.1 ± 16.8 (range = 0–63). The breast surgery sample consisted of 100 women, young or middle aged (mean age = 55.2 ± 12.1 years), scheduled for breast mastectomy (64%) or lumpectomy (36%), all but 2 of whom had no preoperative pain (the 2 exceptions had current intermittent low back pain with an intensity of 3/10 in both cases). A subgroup of women was

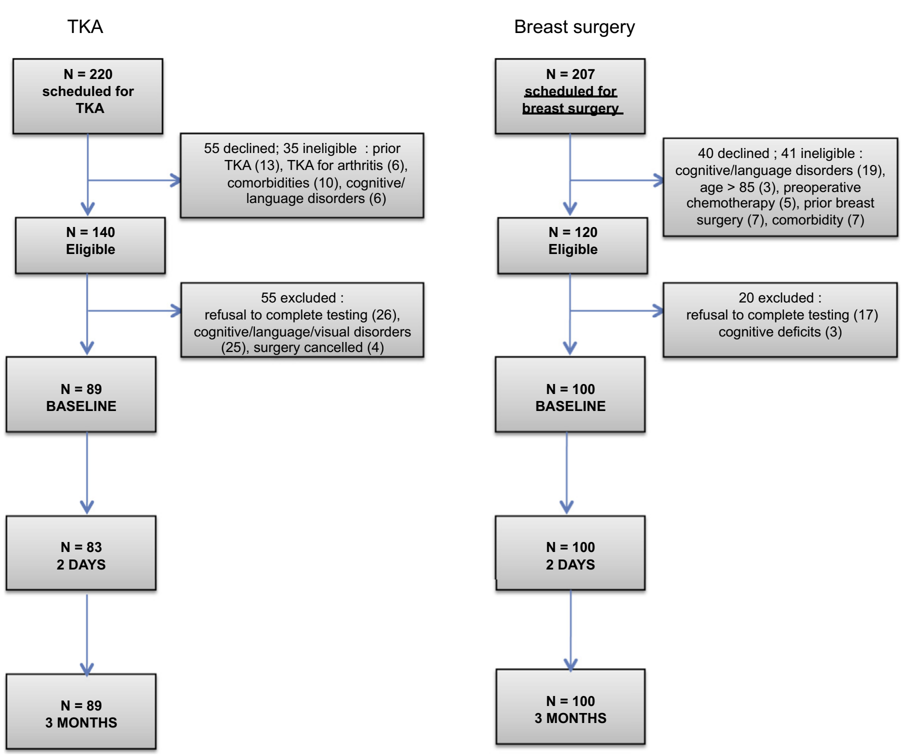

Figure 1. Study flow chart.

Table 1. Demographic, Clinical, and Psychological Variables Before Surgery in the TKA and Breast Cancer Surgery Groups

	TKA	Breast Cancer Surgery
	n = 89*	n = 100
Clinical/demographics		
Sex (women/men) (%)	65/35	100/0†
Age	68.7 ± 8.9 (44–85)	55.2 ± 12.1 (32–80)†
Psychological variables		
Spielberger state anxiety (20–80)	40.5 ± 12.3 (20–69) (n = 88)	45.8 ± 13.5 (21–79)†
Spielberger trait anxiety (20–80)	41.9 ± 8.0 (28–65) (n = 88)	42.0 ± 9.2 (24–71)
BDI (0–39)	4.6 ± 3.9 (0–20)	3.8 ± 3.6 (0–18)
PCS total score (0–52)	19.4 ± 11.2 (0–51)	14.6 ± 11.4 (0–48)‡
PCS magnification (0–11)	3.4 ± 2.9 (0–11)	3.1 ± 2.7 (0–10)
PCS rumination (0–16)	7.2 ± 4.3 (0–16)	5.6 ± 4.4 (0–16)
PCS helplessness (0–25)	8.8 ± 5.6 (0–24)	5.9 ± 5.5 (0–24)‡

Abbreviation: BDI, Beck Depression Inventory.
NOTE. Data are expressed as mean ± SD (range) unless otherwise specified.
*Unless otherwise specified.
†$P < .0001$and ‡$P < .01$ between the TKA and the breast surgical groups.

treated postoperatively, before the 3-month assessment, by radiotherapy (26%) or chemotherapy (61%), according to the same protocol in all cases (5-fluorouracil, epirubicin, and cyclophosphamide every 3 weeks, followed by docetaxel). No woman received hormone therapy during the follow-up period.

Mean depression scores before surgery on the Beck Depression Inventory were in the normal range[3] and similar between groups. By contrast, the scores for state or trait anxiety suggested a moderate level of anxiety in both groups,[43] consistent with previous findings obtained with a similar scale in the same surgical models.[17,23,25] PCS score was higher in the TKA than in the breast model ($P = .004$), with values similar to those previously reported for TKA patients.[38,43,44] In the breast cancer surgery group, PCS total score and the scores of each dimension remained unchanged 2 days after surgery despite acute pain (PCS total score was 13.7 ± 12.1 at 2 days vs 14.6 ± 11.4 at baseline, $P = .3$).

Several significant correlations were found between presurgery variables in each surgical group. The highest correlation coefficients were those obtained for the correlations between state/trait anxiety scores and depression scores (rho = .53–.61, $P < .001$) and between the scores of the 3 dimensions of the PCS (rho = .52–.84, $P < .001$), with similar correlation coefficients in both surgical groups. Moderate correlations were also found between state and trait anxiety scores (rho = .47 and .41 in the TKA and breast surgery groups, respectively, $P < .001$) and between anxiety/depression and PCS magnification/rumination scores, with higher correlation coefficients in the TKA group (rho = .37–.41 in the TKA group, $P < .001$; rho = .28–.36 in the breast group, $P < .05$).

Postoperative Pain Outcome

Pain outcomes at 2 days and 3 months were recorded for both surgical groups (Fig 2). The proportion of patients presenting clinically meaningful pain (Fig 2) and interference with pain on the BPI significantly decreased after TKA surgery ($P < .001$) but remained higher at 2 days and 3 months as compared to the breast group (at 3 months, 50.5% had clinically meaningful pain vs 14% for breast; interference score on the BPI was 21.6 ± 16.1 vs 9.3 ± 10.4 for

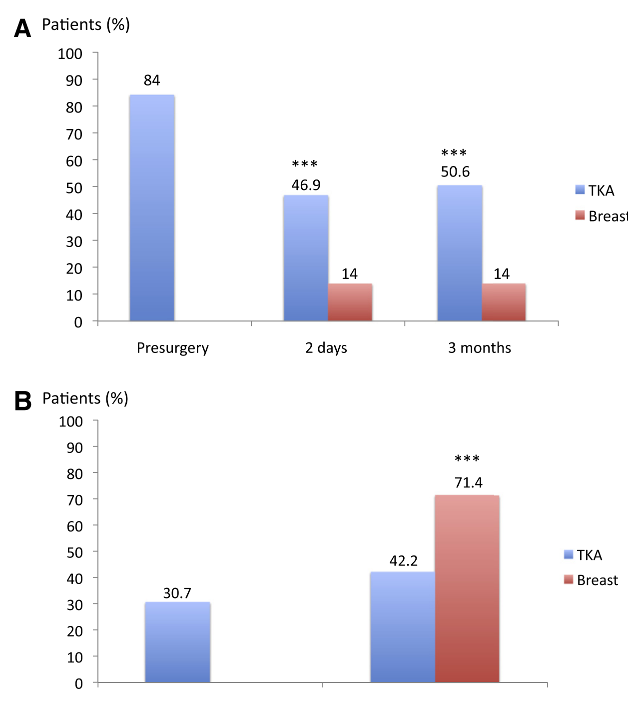

Figure 2. **(A)** Proportion of patients with clinically meaningful pain (based on the average pain intensity on the BPI) in the TKA and breast groups before and 2 days and 3 months after surgery. This proportion significantly decreased 2 days and 3 months after surgery in the TKA group ($P < .0001$) but was higher than in the breast group at both time points ($P < .0001$). **(B)** Proportion of patients with pain and neuropathic characteristics based on the DN4 questionnaire before and 3 months after surgery in the TKA and breast groups. This proportion was significantly higher in the breast group as compared to TKA after surgery ($P < .0001$). ***$P < .0001$ between the TKA and breast cancer surgery groups.

Table 2. Comparison of Somatic and Psychological Variables (Before Surgery or at 2 Days After) in the TKA and Breast Surgery Groups, Between Patients With and Without Clinically Meaningful Pain at 3 Months

	TKA			Breast Cancer Surgery		
	Patients With Pain	Patients Without Pain		Patients With Pain	Patients Without Pain	
Characteristics Before Surgery or at 2 Days	n = 45*	n = 44*	P	n = 14	n = 86	P
Age	69.4 (7.9)	66.5 (9.9)	.06	61.4 (12.3)	54.1 (11.8)	.04
Sex (% women)	69.6	60.4	.34	–	–	–
Radiotherapy (%)	–	–	–	26.7	21.4	.95
Chemotherapy (%)	–	–		42.8	57.1	.25
Pain intensity (BPI)	5.0 (2.1)	4.4 (2.2)	.23	–	–	–
% patients with pain	54	46	.37	–	–	–
Pain at 2 days (BPI)	3.5 (2.8) (n = 44)	2.3 (2.3) (n = 39)	.03	2.1 (1.6)	1.2 (1.1)	.03
Pain duration (years)	15.7 (15.5) (n = 40)	12.7 (11.5) (n = 37)	.47	–	–	–
Trait anxiety	42.7 (7.8)	41.0 (8.1)	.35	47.1 (6.8)	41.2 (9.3)	.02
State anxiety	43.7 (12.1)	34.6 (10.9)	.001	53.7 (11.9)	44.2 (13.0)	.002
BDI	5.4 (4.5)	3.0 (1.9)	.01	5.4 (3.9)	3.4 (3.9)	.06
PCS total	20.3 (11.7)	17.2 (10.3)	.08	16.6 (14.9)	14.3 (10.8)	.47
PCS magnification	3.6 (2.7)	2.7 (2.4)	.09	4.2 (3.2)	2.9 (2.5)	.09
PCS rumination	7.4 (4.4)	6.7 (4.5)	.36	5.7 (5.6)	5.5 (5.7)	.90
PCS helplessness	9.2 (5.9)	7.7 (4.9)	.07	6.6 (6.9)	5.8 (5.8)	.58

Abbreviation: BDI, Beck Depression Inventory.

NOTE. The data shown are mean (SD) unless otherwise specified. Patients with and without pain were compared in Student's t-tests for continuous variables and corrected χ^2 tests for categorical variables.

*Unless otherwise specified.

breast; average pain intensity was 2.9 ± 2.6 vs 1.4 ± 1.5 for breast) (*P* < .001). The high proportion of clinically meaningful residual pain of the operated knee at 3 months in the TKA group has to be viewed in the context of presurgical pain of this knee (84%) and is similar to that reported previously in the same model at the same time point (eg, 44.4% of significant pain at 3 months).[7] By contrast, the proportion of patients with pain in whom neuropathic pain was detected was higher after breast surgery (71% vs 42% for TKA, *P* < .001) because of the higher risk of nerve lesions after breast surgery.[35]

Predictors of the Presence of Clinically Meaningful Postsurgical Pain at 3 Months in the Total Sample of Patients

Step A

Several variables distinguished between patients with and without pain at 3 months, in both groups, with a liberal significance level of *P* < .20 (Table 2). They included state anxiety (*P* < .01), depression score (*P* = .01 and .06 for the TKA and breast surgery models, respectively), the magnification score of the PCS (*P* = .09), acute postoperative pain (at 2 days) (*P* = .03), and age (*P* = .04 and .06 for the TKA and breast surgery groups, respectively).

Step B

In the backward selection (Table 3), several variables emerged as independent predictors of the presence of clinically meaningful pain at 3 months. As expected, the nature of surgery was independently associated with the presence of pain: the odds ratio (OR) for the development of chronic pain was .19 for breast surgery with respect to TKA (*P* < .001), breast cancer surgery being associated with significantly lower levels of pain at 3 months than TKA (see Table 3). Other independent predictors of clinically meaningful pain at 3 months included age (OR = 1.04, confidence interval [CI] = 1.0–1.1, *P* = .03), pain at 2 days (OR = 2.9, CI = 1.3–6.4, *P* = .009), and state anxiety (OR = 1.07, CI = 1.0–1.1, *P* = .001). The CIs for pain at 2 days were larger than those of the other variables, suggesting a lack of precision of the exact estimate of the OR in this case, but values were highly significant. Similar results were obtained in the full statistical model (not shown). Furthermore, this model found no interaction between independent variables and the moderator variable "surgery" (*P* = .3–.9), which shows that the predictive variables are the same whatever the surgical group.

An additional logistic regression analysis in the breast group only, using trait anxiety as an additional independent variable, showed that trait anxiety did not independently predict the presence of clinically meaningful pain (*P* = .19).

Predictors of the Intensity of Postoperative Pain

Step A

Several variables were weakly or moderately correlated with postoperative pain intensity in both surgical groups with a liberal significance threshold of *P* < .20. These included acute pain intensity at 2 days (rho = .29 and .38 in the TKA and breast surgery groups, respectively, *P* < .01), state anxiety (rho = .20, *P* = .06, for TKA; rho = .26, *P* < .001, for breast cancer surgery), Beck

Table 3. Logistic Regression Analysis (Backward Selection) for the Identification of Independent Risk Factors for the Presence of Clinically Meaningful Pain at 3 Months in the Total Sample of Patients (n = 182)

	Total Sample of Patients (Breast, TKA) (N = 182)		
	Odds Ratio	95% Confidence Interval	P
Surgery (breast)	.19	.08–.49	.0006
Age	1.04	1.00–1.08	.03
BDI	.90	.79–1.01	.09
Pain at 2 days (yes)	2.88	1.29–6.38	.009
State anxiety	1.06	1.02–1.10	.0014

Abbreviation: BDI, Beck Depression Inventory.
NOTE. The variables included in regression analyses were those distinguishing between patients with and without pain in both surgical models in analyses of variance, with $P < .20$. Variables: age and state anxiety: continuous variables; pain at day 2: dichotomous variable (yes: pain intensity ≥3/10; no: pain intensity <3/10); surgery: dichotomous variable (breast or TKA).

Depression Inventory score (rho = .20, $P = .06$, for TKA; rho = .17, $P = .08$, for breast cancer surgery), and the magnification score of the PCS (rho = .21, $P = .05$, for the TKA; rho = .19, $P = .06$, for breast cancer surgery).

Trait anxiety was correlated with chronic pain intensity in the breast group only (rho = .19, $P = .06$), whereas PCS total and rumination/helplessness scores were correlated with pain intensity in the TKA group only (rho = .22, $P = .04$, for total score; rho = .22, $P = .04$, for rumination; rho = .19, $P = .07$, for helplessness).

Step B

In the backward selection (Table 4), several variables emerged as independent predictors of pain intensity at 3 months. As expected, the nature of surgery (breast cancer surgery, TKA) was independently predictive of pain intensity ($b = -.93$ for breast cancer surgery vs TKA, $P = .002$), because average pain intensity 3 months after breast cancer surgery was significantly lower than that 3 months after TKA (see Table 3). Other independent predictors of pain intensity were older age ($b = .03$, $P = .005$), state anxiety ($b = .04$, $P = .0001$), PCS magnification score ($b = .14$, $P = .04$), and the presence of pain at 2 days ($b = .96$, $P = .0009$). Similar results were obtained in the full statistical model (not shown). Furthermore, this model found no interaction between independent variables and the moderator variable "surgery" ($P = .4$–$.9$). This shows that the predictive variables make a significant contribution to pain intensity at 3 months, regardless of the surgical model.

In the TKA group, we performed an additional linear regression analysis that showed that total PCS score and scores for other dimensions of the PCS (entered into the model with the above variables) were also independent predictors of pain intensity ($b = .19$, SE = .09, for PCS total score, $P < .01$; $b = .17$, SE = .07, for the helplessness or rumination score, $P < .05$). A regression analysis in the breast group also showed that trait anxiety was not an independent risk factor for chronic pain intensity ($P = .44$).

Predictors of Pain With Neuropathic Characteristics at 3 Months

In total, 59 of the patients in the TKA and breast cancer surgery groups presented clinically meaningful pain at 3 months: 29 developed pain with NC and 30 had pain without NC (see Table 3). Several variables distinguished between the patients with pain who had or did not have NC, at a significance level of $P < .20$, and these variables were entered into multivariate logistic regression analyses. They included age ($P = .12$ between patients with and without pain with NC), pain at 2 days ($P = .11$), depression ($P = .12$), and PCS score ($P = .08$).

In the backward selection (n = 59), the surgical model independently predicted the nature of the pain (neuropathic or non-neuropathic: the OR for the development of pain with NC after breast cancer surgery was 7.83 with respect to TKA (95% CI = 1.8–28.5, $P = .005$) (Table 3). The other independent predictor of the presence of pain with NC was pain at 2 days (OR = 3.82, 95% CI = 1.3–17.4, $P = .02$). By contrast, none of the psychological variables included in the statistical model differentiated between patients with and without pain with NC at 3 months. This was confirmed in the full statistical model (not shown).

Discussion

In this study, we aimed to identify psychological factors predictive of chronic postsurgical pain common to 2 surgical models: TKA for chronic osteoarthritis and breast surgery for cancer. Here we used clinically meaningful pain as an outcome, that is, pain with an intensity ≥3/10 on the BPI. This cutoff corresponds to at least moderate pain with a potential impact on physical or emotional functioning. The surgical models were chosen because they differ considerably in terms of surgical procedure, pain outcome, age and sex of the patients, and the presence or absence of preoperative pain. We considered traditionally used affective and cognitive predictors of postoperative pain, including anxiety and depression (negative affect[30]) and catastrophizing, a cognitive process involving negative thoughts about pain.[47] Such variables were assessed with scales validated for use on subjects with or without pain. We show that regardless of the type of surgery, state anxiety is predictive of the presence of clinically meaningful postsurgical pain and its intensity at 3 months, whereas pain magnification, one of the dimensions of pain catastrophizing, predicts the intensity of postsurgical pain. These variables might represent psychological risk factors for chronic postsurgical pain relevant for all surgical models.

The predictive value of anxiety and catastrophizing for chronic postsurgical pain has been investigated in several studies (see[19,48] for reviews), but all the studies showing positive relationships between these variables and chronic postoperative pain concerned patients with chronic pain before surgery (eg,[2,10,11,13,32,33,40,45,47]). Thus, postsurgical pain in these cases may be a continuation of the presurgical problem rather than new pain generated by surgery.[29] However, 2 studies

Table 4. Linear Regression Analyses (Backward Selection) Aiming to Identify Independent Risk Factors for Pain Intensity at 3 Months (on the BPI) in the Total Sample of Patients Undergoing TKA or Breast Cancer Surgery (n = 182)

Variables	B	Standard Error	T	P
Surgery (breast)	−.93	.30	−3.07	.002
Age	.03	.01	2.82	.005
Pain at 2 days	.95	.28	3.36	.0009
State anxiety	.04	.01	3.88	.0001
PCS magnification score	.14	.05	2.06	.04

NOTE. The variables included in the statistical models were those correlated with pain at 3 months in univariate analyses in both surgical models at $P < .20$. Variables: age, state anxiety, and PCS magnification: continuous variables; pain at 2 days: dichotomous variable (yes: pain intensity ≥ 3/10, no: pain intensity <3/10); surgical model: dichotomous variable (breast or TKA).

specifically analyzed the predictors of "new pain" generated by surgery and reported conflicting results concerning the predictive role of anxiety.[14,32] Only few studies have included patients without preoperative pain and reported no role for anxiety or catastrophizing in predicting postsurgical pain.[18,28] However, in the first of these studies, the patients (young men undergoing chest surgery) developed only mild postsurgical pain,[28] whereas the other study, on patients undergoing breast surgery, included a small sample of patients (n = 24) and considered an outcome of mild to severe postoperative pain,[18] which may be less relevant than the clinically meaningful pain used here. We show here that state anxiety and pain magnification are predictive of chronic clinically meaningful postoperative pain, regardless of the presence or absence of preoperative pain, confirming that these psychological variables are associated with a higher risk of new pain generated by surgery rather than simply with the persistence of chronic pain.

No study has simultaneously investigated the potential independent predictive value of state and trait anxiety, catastrophizing, and depression for chronic postsurgical pain. Our results showing that state anxiety and catastrophizing independently predict chronic postsurgical pain, despite significant correlations before surgery, extend previous findings for acute postoperative pain.[15,34] They confirm that state anxiety and catastrophizing are different dimensions of the experience of pain.[15] By contrast, trait anxiety did not emerge as an independent predictor of chronic pain in our study, consistent with most previous studies (refs in[48]). Like trait anxiety, depression, despite its association with chronic pain in univariate analyses, had no independent impact on either the prevalence or the severity of chronic postsurgical pain, consistent with previous findings for the TKA model.[45,47] The low baseline scores for depression in our population may account for these results, although we cannot rule out the possibility that depression, at least in severe cases, makes an independent contribution to chronic postsurgical pain (refs in[19]).

Pain catastrophizing, as assessed by the PCS, has been developed as a multidimensional construct comprising elements of magnification, rumination, and helplessness.[44,45,47] In our study, only pain magnification—a heightened perception of the threat represented by pain symptoms[47] —emerged as a significant predictor of chronic pain intensity, even in patients with no preoperative pain. This suggests that the anticipation of strong pain in the absence of current pain symptoms may have the same negative consequences as that in patients currently experiencing pain. Interestingly, functional MRI studies have shown that pain anticipation activates cerebral regions involved in or close to regions involved in the experience of pain.[35,37,42,50] Furthermore, the anticipation of strong pain has been reported to elicit a shift in cerebral brain activity from the ventromedial prefrontal cortex, which is involved in anticipation, to the periaqueductal gray matter, which is involved in pain modulation.[31] Unlike pain magnification, rumination and helplessness were predictive of chronic postsurgical pain in the TKA model only, consistent with previous findings.[45,46] This suggests that these dimensions of catastrophizing may be more specific to some surgical models than pain magnification.

We also assessed the predictive value of somatic variables for clinically meaningful postsurgical pain at 3 months after breast cancer surgery and TKA. Acute pain severity made a major contribution to chronic pain severity and prevalence, consistent with previous findings.[1,18,25,32,33,38] However, baseline pain intensity was not predictive of pain after TKA, contrasting with previous findings for this model.[40,45,46] One reason for this discrepancy may be that the pain outcome measure used here (average pain intensity in the BPI), to allow comparisons with the breast cancer surgery model, is less sensitive than the Western Ontario and McMaster Universities Arthritis Index for determining the specific nature of osteoarthritis pain before surgery.[4] Finally, we found that older age of the patient was predictive of postsurgical pain, although this effect was more significant in the TKA model. These data go against previous findings suggesting that a younger age of the patient is associated with higher levels of pain after surgery.[23,26,34,36] However, the apparent protective effect of older age in these studies mostly concerned acute postsurgical pain (eg,[23,34]) and pain after breast cancer surgery.[26,36] Furthermore, after breast surgery,[26,36] younger age of the patient has been shown to be predictive of postsurgical pain of any intensity, including mild pain, but not specifically of moderate to severe pain, the outcome used in our study.

Breast surgery and TKA induce different types of postoperative pain. Neuropathic pain has been reported more commonly after breast surgery[39,49] than after knee surgery.[51] We found that most painful patients undergoing breast surgery had pain with NC, as assessed by the 7-item DN4 questionnaire (71%), whereas such pain occurred in less than 50% of the painful patients undergoing knee surgery. In multivariate analyses, acute pain was the only variable specifically predictive of pain with NC (the psychological variables were not predictive). These data suggest that somatic factors are of greater predictive value than psychological factors for the occurrence of neuropathic pain. Psychological factors seem to have similar effects on the likelihood of chronic postsurgical pain regardless of the nature of that pain.

One of the major strengths of our study is the consideration of a large group of consecutive patients scheduled for TKA or breast surgery for inclusion and the completion of the 3-month assessment for all the patients. However, this study was also subject to limitations. We used stringent inclusion criteria for this study to maximize the homogeneity of the sample for each surgical model. This may limit the generalization of our data to a broader range of patients undergoing surgery. However, the characteristics of the patients included were similar to those reported in previous studies on patients undergoing TKA[45,46] or breast surgery.[12,36] Another potential limitation concerns the small number of affective and cognitive factors studied here, which do not encompass all the diverse potential psychosocial predictors of chronic postsurgical pain, including stress, hypervigilance, psychological vulnerability, and negative expectations.[22,28,33] Finally, because we limited our data to a 3-month time point that marks the onset of chronic postsurgical pain, we cannot exclude the possibility that the factors identified here predict the transition to pain chronicity rather than the maintenance of pain over longer periods of time, as has been reported previously.[22]

This study has implications for clinical practice. We found that a combination of somatic (acute pain) and psychological factors (anxiety and pain magnification) increased the risk of chronic pain, regardless of the surgical model, which is consistent with previous findings.[8,13,32,33] Despite the use of high levels of analgesics, particularly in the TKA group, almost half the patients in this group experienced clinically meaningful postsurgical pain 2 days after surgery. This highlights the need to optimize the management of acute postoperative pain. Our findings also suggest that patients scheduled to undergo any type of surgery should be screened for state anxiety and catastrophic thinking. In particular, the magnification subscale of the PCS, which is easy to assess, could be used as a screening test before surgery. However, it remains to be determined whether the management of dysfunctional pain cognition (by cognitive-behavioral therapy, for example), can actually decrease the risk of chronic postsurgical pain.

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