



Published in final edited form as:

J Pain Symptom Manage. 2010 June ; 39(6): 1043–1052. doi:10.1016/j.jpainsymman.2009.11.318.

Pre-Surgery Psychological Factors Predict Pain, Nausea and Fatigue One Week Following Breast Cancer Surgery

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Abstract

Prior to scheduled surgery, breast cancer surgical patients frequently experience high levels of distress and expect a variety of post-surgery symptoms. Previous literature has supported the view that pre-surgery distress and response expectancies are predictive of post-surgery outcomes. However, the contributions of distress and response expectancies to post-surgical side effect outcomes have rarely been examined together within the same study. Furthermore, studies on the effects of response expectancies in the surgical setting have typically focused on the immediate post-surgical setting rather than the longer term. The purpose of the present study was to test the contribution of pre-surgery distress and response expectancies to common post-surgery side effects (pain, nausea, fatigue). Female patients ($n=101$) undergoing breast cancer surgery were recruited to a prospective study. Results indicated that pre-surgery distress uniquely contributed to patients' post-surgery pain severity ($P<0.05$) and fatigue ($P<0.003$) one week following surgery. Response expectancies uniquely contributed to pain severity ($P<0.001$), nausea ($P<0.012$) and fatigue ($P<0.010$) one week following surgery. Sobel tests indicated that response expectancies partially mediated the effects of distress on pain severity ($P<0.03$) and fatigue ($P<0.03$). Response expectancies also mediated the effects of age on pain severity, nausea and fatigue. Results highlight the contribution of pre-surgery psychological factors to post-surgery side effects, the importance of including both emotional and cognitive factors within studies as predictors of post-surgery side effects, and suggest pre-surgical clinical targets for improving patients' postoperative experiences of side effects.

Keywords

Response expectancies; surgery; breast cancer; side effects; pain; nausea; fatigue

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Introduction

Surgery is an essential part of all current treatments to cure breast cancer. Over 90% of women diagnosed with breast cancer undergo operative treatment (1), with a trend toward more patients receiving breast conserving surgery (2,3). However, cure is not without its price. Pain, nausea, and fatigue are particularly severe problems following breast cancer surgery (4–8). In addition to being highly aversive to patients, post-surgery pain and nausea can significantly impact recovery from breast surgery, requiring pharmacologic intervention, prolonging recovery room stay, delaying discharge, and leading to unanticipated readmissions (5–9). Fatigue is also a significant problem following breast conserving surgery, affecting the vast majority of patients (4,10,11). Cancer patients report that fatigue has a greater negative impact on daily activities than other cancer-related symptoms (12).

Although medically necessary, both excisional breast biopsy and breast conserving surgery (e.g., lumpectomy) can be emotionally taxing for women. Research has consistently found elevated levels of distress in these patients (13–19). Such distress is multiply determined, resulting from factors including: concerns about changes in appearance and scarring (20), concerns about anesthesia (21), concerns about surgical procedures (e.g., pain during procedure, postoperative side effects) (22), and concerns about diagnosis and prognosis (23).

Regardless of its source, pre-surgery emotional distress has been linked to patients' subsequent experiences of post-surgery side effects. For example, pre-surgery distress has been found to predict post-surgery pain (24–31); post-surgery nausea (6,32) and post-surgery fatigue (33,34) across a broad spectrum of surgeries. Within breast cancer surgical patients, pre-surgery distress also appears to be a harbinger of subsequent post-surgery side effects (31,35).

In addition to distress, response expectancies are a second psychological factor likely to contribute to patients' experiences of side effects following breast surgery (35). Response expectancies (36,37) are specific expectations for non-volitional outcomes, rather than expectations for behaviors or external events. For example, an expectation that one will experience pain after surgery would be considered a response expectancy, while an expectation that one will be able to lift one's arm or that it will rain today would not. Response expectancies are thought to reflect automatic (i.e., typically not under voluntary control) processes. According to Response Expectancy Theory, expectancies contribute to outcomes. In terms of surgery, expectancies that one will feel pain, nausea, or fatigue should directly contribute to experiences of these phenomena (36). The literature has supported Response Expectancy Theory across various settings (see reference 38)). A recent meta-analysis in the cancer setting (39) revealed a significant ($Z = 6.58$, $P < 0.001$) medium-sized ($r = 0.36$) association between patients' response expectancies for cancer-treatment-related side effects and the experience of these side effects. More specifically, within the cancer surgical setting, expectancies have been shown to predict cancer patients' experiences of nausea, pain, and fatigue at ambulatory surgical discharge (35). To date, the literature has focused on expectancy effects in the immediate postoperative period, and the relationship between expectancies and more persistent side effects (e.g., one week following surgery) is not known. Given that expectancies for side effects are commonly held by cancer patients (40), their effects on pain, nausea and fatigue one week following surgery deserve further study.

Response Expectancy Theory also predicts that the relationship between expectancies and outcomes will not be perfectly mediated (41) by another psychological variable. That is, expectancies should predict side effects, and the relationship between the expectancy and the

side effect outcome should not be fully accounted for by other psychological variables (e.g., emotional distress). Data demonstrating that an effect due to response expectancies was perfectly mediated by another psychological variable would be inconsistent with Response Expectancy Theory.

The purpose of this study was to test the contribution of patients' pre-surgical response expectancies and emotional distress to patients' experiences of post-surgical pain, nausea and fatigue one week following breast cancer surgery. In the present study, we planned to test the hypotheses that pre-surgery expectancies and distress would predict post-surgical pain, nausea and fatigue one week following surgery. Additionally, consistent with Response Expectancy Theory (42), we also hypothesized that in no instance would distress perfectly mediate (41) the effects of expectancies on side effect outcomes. The results of the study will increase our understanding of the psychological factors contributing to breast cancer surgical patients' experiences of post-surgical side effects, and in doing so, will guide the development of future interventions to ameliorate these side effects.

Methods

Participants

All participants were female ($n=101$; M age = 49.43 years, SD = 14.06 years). The present sample overlaps with control group patients described in a previous publication focused on the effects of a psychological intervention (43). Eligible patients were those scheduled for breast conserving surgery for cancer diagnosis or for cancer treatment (excisional breast biopsy or lumpectomy). Eligibility criteria also included the ability to speak and read English (as the study forms were in English). Patients were ineligible if they were scheduled for mastectomy, as their recovery from surgery is quite different from women undergoing breast conserving surgery. Patients also were ineligible if they had any uncontrolled major comorbid mental or physical illness (determined by chart reviews), as such a factor could bias the data for those individuals.

Patients were contacted for participation following notification that they were to be scheduled for breast cancer surgery. Seventy-five percent of eligible patients contacted agreed to participate in the study. The most frequent reason for declining was difficulty understanding English (9%), followed by patients feeling that they were already overwhelmed and did not want to add any responsibilities to their lives (8%). Six percent refused to participate due to scheduling conflicts, and 2% had their surgery cancelled. All participants provided written informed consent according to Mount Sinai School of Medicine Institutional Review Board guidelines. Sixty-one percent of the sample described themselves as Caucasian, 14% as African American, 12% as Hispanic, 4% as Asian (9% as Other); 50% of the sample was married. With regard to education, 25% did not hold a college degree, 44% graduated from a four-year college, and 31% had at least some graduate school/professional training.

In order to recruit a homogeneous sample with regard to postoperative recovery, eligible patients had to be scheduled for ambulatory breast conserving surgery, either excisional breast biopsy (70%) or lumpectomy (30%). These two procedures differ only in the greater surgical margin taken with the latter, to ensure full resection of malignant tissue (44). That is, if there is a known cancer, slightly more healthy tissue is excised during lumpectomy, relative to excisional breast biopsy, to improve the probability of removal of all cancerous cells. With regard to post-surgery cancer diagnosis/stage, 65% of the sample were cancer negative, 9% were Stage 0, 17% were Stage I, and 9% were Stage II.

Operative procedures (surgical and anesthetic) followed uniform institutional guidelines. All patients followed the same anesthetic protocol for monitored anesthesia care. Breast conserving surgical procedures were accomplished under local anesthesia (lidocaine 2% with 1:100,000 epinephrine), which was supplemented with an intravenous sedation regimen to achieve an Observer's Assessment of Alertness/Sedation (OAA/S) score between 2 and 4 (45). Sedation was achieved with combinations of short acting narcotic agents (fentanyl 0.5–2 µg/kg infusion at 0.01–0.05 µg/kg/min) and sedative hypnotic agents (midazolam 0.01–0.1 mg/kg, and/or propofol 10–50 µg/kg/min). Consistent with standard Mount Sinai practices, patients were prescribed analgesics upon discharge (both opioid and non-opioid). All patients were scheduled to be discharged from the hospital on the same day as their procedure. The use of postoperative pain medication was self-reported by participants.

Measures

Pre-Surgery Measures—Demographic information (age, ethnicity, education, marital status) was collected with a brief questionnaire. Medical information (type of surgery, diagnosis, stage of disease) was collected via chart review.

Pre-surgery distress was assessed using the tension-anxiety subscale of the short version of the Profile of Mood States (SV-POMS) (46). The scale has demonstrated reliability and validity with breast cancer patients (46), as well as excellent internal consistency within our sample (Cronbach's alpha = 0.91). The tension-anxiety subscale has six items which were rated on a 0 (not at all) to 4 (extremely) scale.

Pre-surgery expectancies for pain, nausea and fatigue were assessed using 100 mm visual analogue scales (VASs). Each expectancy item followed the same format. For example, the expectancy item for pain stated, "After surgery, how much pain do you think you will feel? Please put a slash through this line (shown below on the actual forms) to indicate how much pain you expect to feel." The line is anchored by "No pain at all" and "As much pain as there could be." The VAS format for expectancies is particularly useful in busy medical settings where patient burden and time constraints are common concerns, and has been used in the cancer surgical setting (16,35,47).

Post-Surgery Measures—Post-surgery pain was assessed using the pain severity subscale of the Brief Pain Inventory (48). The pain severity subscale consists of three items rated on a 0–10 numerical rating scale. These items assess patients' worst pain over the past week, average pain over the past week, and pain right now. The pain severity score is derived by summing these three items. The BPI has previously demonstrated strong reliability and validity (49,50), and has been widely used with a variety of surgical patient populations (8,51,52), including breast surgery (53). Internal consistency for the pain severity score within our sample was excellent (Cronbach's alpha = 0.90).

Post-surgery nausea was assessed using a 100 mm VAS. VAS measurement of nausea in breast cancer patients is both common and well-established (35,43). The VAS item read, "During the past week, how nauseated have you felt?" The item was anchored by "Not at all nauseated" and "As nauseated as I could be." Participants were instructed to answer this VAS nausea item as described above for the expectancy items.

Post-surgery fatigue was assessed using the fatigue-inertia subscale of the SV-POMS. The scale contains five items, and has demonstrated reliability and validity with breast cancer patients (46), as well as excellent internal consistency within our sample (Cronbach's alpha = 0.92). Items were summed to derive the total fatigue score, which can range from 0 to 20. Each of the five items were rated on a 0 (not at all) to 4 (extremely) scale.

Procedure

Prior to surgery, patients completed the demographic items at home. In the clinical waiting area on the morning of surgery (prior to surgery), patients completed the tension-anxiety subscale of the SV-POMS, and VAS measures of expectancies for: post-surgery pain, nausea, and fatigue. A research assistant was present to answer any questions patients had about the assessment materials. For administration of all VASs, the research assistant explained that a mark closer to the left end of the line indicated less of the variable in question, and a mark further to the right indicated more. All patients were asked if they understood how to complete VAS scales before providing their responses. One week following breast surgery, all patients completed pain, nausea and fatigue measures at their one-week clinical follow-up with their surgeon, collected by a research assistant. At this time, patients also reported on analgesic medication used during this one-week period.

Statistical Analyses

Prior to inferential statistics, the distribution of each variable was checked. There were no gross violations of normality (all skewness and kurtosis values were within ± 2) (54) with the exception of postsurgery nausea, which was leptokurtic (kurtosis = 8.58). Therefore, we used a square root transformation (54), which brought the skewness and kurtosis values to within ± 2 . Statistical analyses were conducted using techniques for multiple regression and correlation using SAS (55).

Results

To determine whether demographic or medical factors contributed to the outcomes, such factors were entered as predictors of post-surgery side effects (pain, nausea and fatigue). None of the demographic or medical variables (education, ethnicity, marital status, type of surgery, stage of disease) predicted pain, nausea or fatigue (all P s > 0.10), with the exception of age and pain medication used during the week following surgery. Age was a significant predictor of each of the outcomes (P s < 0.05), and was included as a predictor in subsequent analyses. In all cases, age was negatively correlated. Pain medication (coded as none = 66% of patients, non-opioid = 17% of patients, opioid = 17% of patients) predicted pain severity [$F(2, 98) = 3.59, P < 0.04$], but not nausea [$F(2, 98) = 0.18, P < 0.84$] or fatigue [$F(2, 98) = 1.45, P < 0.24$]. Patients who did not take pain medications had a mean pain severity score of 7.21 (SD=5.63); those who took non-opioid medications had a mean pain severity score of 9.94 (SD=5.06) and those who took opioid medications had a mean pain severity score of 11.00 (SD=7.52). In order to make statistical comparisons between these groups of patients, we used Tukey tests to control for the overall family-wise error rate. Without such a control, one would be more likely to incorrectly detect significant differences when making multiple comparisons between groups. Post-hoc Tukey tests indicated that pairwise differences between type of pain medication (none, non-opioid, opioid) on pain severity scores were all non-significant ($P > 0.05$). Means and standard deviations of pre- and post-surgery psychological and side effect variables are presented in Table 1.

Table 2 depicts the bivariate correlations between the pre-surgery and one week post-surgery outcomes. Age is also included as a variable. Bivariate analyses indicate that the older a person is, the less pain, nausea and fatigue they were likely to experience. Correlations between pre-surgery distress and post-surgery outcome variables, and between pre-surgery specific expectancies and their associated outcomes variables were significant and positive with the exception of the relations between distress and nausea.

In order to test the independent contributions of pre-surgery emotional distress and expectancies to post-surgery outcomes, a series of multiple regression analyses were conducted. As age was a significant predictor of each of the outcomes in bivariate analyses, it was included as a predictor in these equations. Pain medication use was included in the prediction of pain severity. All predictive models were significant: *Pain severity*: $F(4, 96)=9.33, P < 0.0001$, Total Model R-squared = 0.28; *Nausea*: $F(3, 97)=6.37, P < 0.0006$, Total Model R-squared = 0.16; *Fatigue*: $F(3, 97)=10.77, P < 0.0001$, Total Model R-squared = 0.25. In order to evaluate the magnitude of the contribution of psychological factors alone, age and pain medication were removed from the statistical models. These analyses revealed that response expectancies and distress together explained 28% of the variance in pain severity; 11% of the variance in nausea; and 25% of the variance in fatigue. To determine the unique contributions of all predictors to the outcomes, standardized parameter estimates and squared semipartial correlations are also reported (Table 3).

Multiple regression analyses (Table 3) revealed that response expectancies uniquely contributed to patients' experiences of pain, nausea, and fatigue at one week post-surgery. Also, in no instance were the effects of response expectancies perfectly mediated (41) by pre-surgery distress, consistent with Response Expectancy Theory (36). As the literature suggests that emotional distress is a source of patients' expectations prior to surgery (47), we then explored whether response expectancies mediated the effects of distress and age on the post-surgery outcomes. Perfect mediation by expectancies was demonstrated for the effects of age on patients' pain severity following surgery. In order to test the statistical significance of the independent variables (e.g., distress) on the dependent variables (e.g., post-surgery pain severity) via the mediator (expectancy) where there was the potential for partial mediation, we used a Sobel test. Partial mediation by expectancies was demonstrated for: 1) the effects of pre-surgery distress on pain severity (Sobel test statistic = 2.16, $P < 0.03$); 2) the effects of pre-surgery distress on post-surgery fatigue (Sobel test statistic = 2.14, $P < 0.03$); 3) the effects of age on post-surgery nausea (Sobel test statistic = -1.96, $P < 0.05$); and 4) the effects of age on post-surgery fatigue (Sobel test statistic = -2.22, $P < 0.03$).

Discussion

We hypothesized that both response expectancies and distress would predict patients' experiences of pain, nausea and fatigue one week following breast cancer surgery. Bivariate results were consistent with these hypotheses, as well as with the empirical literature (39). Multiple regression analyses revealed that the hypothesized psychological factors (response expectancies and distress) explained significant amounts of variance in one week post-surgery pain (28%), nausea (11%), and fatigue (25%). These results provide strong evidence for the role of pre-surgery psychological factors in determining experiences of symptoms one week after an invasive surgical procedure. In short, a quarter of patients' pain and fatigue were determined by psychological factors. The analyses further revealed that in all instances response expectancies continued to make a unique contribution to post-surgery side effects after accounting for pre-surgery emotional distress. This result is consistent with the tenet of Response Expectancy Theory that expectancy effects are not completely accounted for by other psychological variables (36). The results also suggest that response expectancies are a mediator of the effects of emotional distress on post-surgery pain and fatigue. These results highlight the importance of expectancies and distress in investigations of pre-surgery psychological influences on post-surgery outcomes. Medical and demographic factors did not account for these effects.

From the clinical perspective, the results suggest that patients with higher pre-surgery levels of expectancies and emotional distress appear to be at greater risk for experiencing higher levels of post-surgery side effects. Clinicians should be cautious of how they describe

potential side effects of surgery, and should be attuned to managing expectancies and distress prior to surgery. For example, while properly informing patients concerning the risks of procedures, clinicians should avoid overgeneralizing or overemphasizing negative experiences in initial consultations (e.g., all patients will have high levels of pain). Instead, clinicians should consider emphasizing potential individual differences, where appropriate, in patient responses to surgery (e.g., some patients have little pain, while others have more, everyone is different). Such a communication style is likely to allay fears (reduce distress) as well as set more positive and realistic expectancies.

Additionally, psychological interventions that can alter both patients' expectancies and distress prior to surgery may be particularly effective for controlling side effects following surgery. One such intervention is hypnosis (56). Hypnosis has the benefit of not only being effective for changing expectations (36) and reducing distress (57,58), but also being brief, which can be critical in the hectic surgical environment. Furthermore, hypnosis has been demonstrated to be effective with a wide variety of surgical patients across a wide variety of outcomes (43,59).

The present results are consistent with the published breast cancer surgery literature. In a separate sample, our group reported that both distress and expectancies predicted pain, nausea and fatigue at hospital discharge following ambulatory (same day discharge) breast cancer surgery (35). The present manuscript extends those findings to one week following surgery, further supporting the importance of pre-surgery expectancies and distress as determinants of patients' longer-term experiences of side effects. The present study extends the research literature on breast cancer surgical patients by incorporating both cognitive (response expectancies) and emotional (distress) elements as predictors, rather than focusing on emotion exclusively (31). Thus, the results of the present study describing the relative contributions of response expectancies and distress are novel.

An interesting finding of the present study was that older age predicted lower levels of postsurgical side effects (conversely, younger age predicted higher levels of postsurgical side effects), regardless of whether the outcome was pain, nausea or fatigue. Mediation analyses indicated that expectancies accounted at least in part for the effects of age on post-surgery side effects. This is consistent with previous literature demonstrating a negative correlation between age and expectancies for side effects (40,47,60). These results might be explained by Social Learning Theory (61), which suggests that increased experience with a situation shapes one's expectancies in that context. In the present case, we can speculate that perhaps older patients are more likely to have had previous personal or vicarious experience with surgery, which has influenced their expectancies for side effects. The literature has supported a link between medical experience and expectancies for side effects in breast cancer chemotherapy patients (62). However, in the present study we do not have the necessary data on patients' side effect experiences associated with previous personal medical histories to test this possibility across various ages, and therefore this possibility must be viewed with caution at this time. Regardless, clinicians may wish to be aware that younger patients may be at greater risk for more severe symptoms, and possibly in greater need of intervention.

No study is without limitations, and the present study is no exception. First, personality characteristics were not included in our study design, and they could potentially moderate some of the effects reported here. However, the literature has demonstrated that personality factors (e.g., optimism, trait anxiety) are often important contributors to pre-surgery distress and expectancies rather than vice versa (17,47,63). That is, they are upstream from the more proximal predictor variables examined here, and potentially less amenable to intervention. Second, we considered the possibility of imposing a clinical cutoff on our outcome variables

(i.e., imposing “caseness”) through dichotomization of each side effect outcome. We chose not to do so for two reasons: a) dichotomizing continuous data is contrary to statistical recommendations, and can potentially yield misleading results (64,65), and b) from a more empathic and humanistic perspective, we believe that each patient’s symptom experience is valid and clinically meaningful to them. Third, these results are limited to patients undergoing breast cancer surgery, and should be replicated in other populations.

In conclusion, the data support the contribution of both response expectancies and emotional distress to the prediction of breast cancer surgical patients’ experiences of post-surgery side effects. These data are consistent with Response Expectancy Theory (36) and supportive of the development of pre-surgery psychological interventions which can reduce pre-surgery response expectancies and distress, in service of reducing post-surgical side effects and improving recovery.

Acknowledgments

This work was supported by the National Cancer Institute (R25CA129094; K07CA131473) and the American Cancer Society (RSGPB CPPB-108036). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Cancer Institute or the National Institutes of Health.

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Table 1Means and Standard Deviations (SD) of the Study Variables ($n=101$).

Variable (possible range)	Mean	SD
Presurgery		
Pain Expectancy (0–100)	44.79	24.82
Nausea Expectancy (0–100)	34.25	27.75
Fatigue Expectancy (0–100)	54.49	27.29
Distress (0–24)	10.43	5.98
One Week Postsurgery		
Pain severity (0–30)	8.31	6.04
Nausea (0–10) ^a	1.87	2.76
Fatigue (0–20)	7.51	5.65

^aThese values represent the square root transformed data.

Table 2

Correlations Between Predictors and One-Week Side Effect Outcomes ($n=101$).

Measure	1	2	3	4	5	6	7	8
1. Age	-							
2. Pain Expectancy	-0.26 ^b	-						
3. Nausea Expectancy	-0.23 ^c	0.36 ^b	-					
4. Fatigue Expectancy	-0.20 ^c	0.27 ^d	0.40 ^e	-				
5. Distress	-0.18	0.19 ^f	0.14	0.25 ^c	-			
6. Pain Severity	-0.26 ^d	0.47 ^e	0.30 ^d	0.22 ^c	0.28 ^d	-		
7. Nausea ^a	-0.31 ^d	0.20 ^c	0.31 ^d	0.30 ^d	0.17	0.27 ^d	-	
8. Fatigue	-0.29 ^d	0.05	0.10	0.35 ^e	0.38 ^b	0.36 ^b	0.37 ^e	-

^aThe square root transformed variable was used to compute these statistics.

^b $P < 0.0001$.

^c $P < 0.05$.

^d $P < 0.01$.

^e $P < 0.00001$.

^f $P < 0.06$.

Table 3Predictors of One-Week Postsurgery Pain, Nausea, and Fatigue ($n=101$).

Outcome	Predictors	Standardized Parameter Estimate ^a	Squared Semipartial Correlation	<i>P</i> <
Pain Severity	Age	-0.12	0.01	0.196
	Pain Medication	0.12	0.02	0.175
	Distress	0.17	0.03	0.054
	Expectancy	0.37	0.11	0.001
Nausea	Age	-0.23	0.05	0.018
	Distress	0.10	0.01	0.317
	Expectancy	0.25	0.06	0.012
Fatigue	Age	-0.19	0.03	0.042
	Distress	0.29	0.08	0.002
	Expectancy	0.24	0.05	0.010

^aStandardized parameter estimates, squared semipartial correlations, and associated *P*-values reflect unique variance accounted for in the dependent variables accounting for all other predictors.