Predictive Factors for Patients who Need Treatment for Chronic Post-Surgical Pain (CPSP) after Breast Cancer Surgery

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Research Article

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Abstract

Purpose: Although chronic postsurgical pain (CPSP) after breast cancer surgery is a common and prevalent postsurgical adverse event, the need for CPSP treatment has not been investigated. This study examined the proportion of patients who needed treatment for CPSP and associated predictors.

Methods: We conducted a cross-sectional study with female patients who underwent breast cancer surgery at our institution. Participants were aged ≤65 years at the time of this study and were at least 1 year post surgery. The questionnaire examined the presence of and need for treatment for CPSP and included the Japanese version of the Concerns about Recurrence Scale (CARS-J). Multivariate analyses were used to identify independent predictors of needing treatment for CPSP.

Results: In total, 305 patients completed the questionnaire. The mean time since surgery was 67.1 months; 151 (51%) patients developed CPSP after breast cancer surgery and 61 (39%) needed treatment for CPSP. Among patients that developed CPSP, the fear of breast cancer recurrence as assessed by the CARS-J (odds ratio [OR] 2.22, 95% confidence interval [CI]: 1.30–3.81, *P*=0.004) and ≥2 postsurgical pain regions (OR 2.52, 95% CI: 1.16–5.57, P=0.020) were independent predictors of needing treatment for CPSP.

Conclusions: This study is the first to identify the proportion and predictors of patients who need treatment for CPSP. Fear of breast cancer recurrence and ≥2 postsurgical pain regions may predict the need for CPSP treatment among patients following breast cancer surgery.

Introduction

Breast cancer is the most prevalent malignancy in women and its incidence is increasing[1]. Patients with breast cancer are living longer as a result of improvements in systemic treatment[2, 3], which highlights the importance of maintaining a good quality of life (QOL)[4].

Chronic postsurgical pain (CPSP) is a major clinical problem that affects about half of patients after breast cancer surgery[5–7]. This pain may persist for several years or be permanent[8]. CPSP after breast cancer surgery has been reported to interfere with multiple aspects of life[9], adversely affect QOL, and cause profound psychological distress[9–11]. Predictors of CPSP after breast cancer surgery include younger age, type of surgery, and acute postsurgical pain[5, 6]. Although CPSP is a common and prevalent postsurgical adverse event after breast cancer surgery, the characteristics of patients who need treatment for CPSP have not been identified.

Despite the improved treatments and prognosis for breast cancer, some patients with breast cancer develop recurrence or metastasis after treatment. We previously reported that the most prevalent unmet need among breast cancer survivors was the “fear of cancer spread”; more than half of those patients needed help to alleviate this fear[12]. The fear of cancer recurrence was also reported to be strongly associated with postsurgical pain[13] and lower QOL among breast cancer survivors[14].

To reduce the number of patients who suffer from CPSP after breast cancer surgery, it may be beneficial to identify patients at high-risk who need treatment for CPSP and provide treatment for these patients early in the postsurgical period. Given that the fear of cancer recurrence and disability in daily life were strongly associated with CPSP and low QOL, we hypothesized that these factors may predict patients who need treatment for CPSP. The purpose of this study was to investigate the proportion of patients who needed treatment for CPSP and associated predictors, especially the influence of the fear of cancer recurrence or disability in daily life due to pain.

Methods

Study Design And Participants

This single-institution cross-sectional study included 305 ambulatory female patients who had undergone surgery for breast cancer between 1988 and 2019. These patients attended the outpatient clinic at the Department of Breast Surgery at Nagoya City University Hospital in Japan. The eligibility criteria for inclusion in this study were: 1) patients who underwent breast cancer surgery at our institution, 2) patients who were disease-free survivors at least 1 year after breast cancer surgery, and 3) patients aged ≤ 65 years at the time of this study. We restricted the age of participating patients because younger age has been reported to be a predictor of CPSP[5] and the patient questionnaire was completed using an iPad (Apple Inc., Cupertino, CA, USA). The exclusion criteria were: 1) patients with severe pain due to diseases other than breast cancer, 2) patients who were treated for synchronous cancers or metachronous cancers, and 3) patients considered physically or mentally incapable of participation by their oncologists.

Procedure

Eligible patients were listed in advance and briefed about the study by their physician at the time of their outpatient visit. After informed consent had been obtained, patients were asked to complete the study questionnaire using an iPad at the hospital. The protocol for this study (60-19-0031) was approved by the Institutional Review Board of Nagoya City University Graduate School of Medical Sciences. This study conformed to the guidelines of the Declaration of Helsinki.

Data Collection

Demographic data and patient characteristics such as age (currently and at the time of surgery), time (months) since surgery, body mass index (BMI), type of surgery and reconstruction, stage of breast cancer at diagnosis, and type of adjuvant treatment were retrieved from patients' medical records. A self-administered questionnaire was used to obtain additional information such as overall fear of breast cancer recurrence, pain severity and pain interference with life, distribution of postsurgical pain regions, use of analgesics after surgery, presence of psychiatric disorders, presence of family members, tobacco

use, and alcohol intake. The presence of CPSP and need for treatment of CPSP were assessed with specific questions: 1) “Where is CPSP present?” (surgical site, axilla, arm, no pain) and 2) “Is there need for treatment of CPSP?” (yes, depends on the treatment, no). CPSP was defined as present when a patient selected one of the listed options (i.e., surgical site, axillary, arm). The need for CPSP treatment was defined as when a patient selected one of the listed options (i.e., yes, depends on treatment). The information obtained from the questionnaire was linked to the clinical information obtained from patients’ medical records.

Overall fear of breast cancer recurrence assessed by the Japanese version of the Concerns About Recurrence Scale (CARS-J)

The CARS is a 30-item breast cancer-specific self-report scale, originally developed in the USA[15]. It assesses the overall fear of breast cancer recurrence and covers four specific domains. Responses are on a scale from 0 to 6, with higher scores indicating greater overall fear of breast cancer recurrence. After obtaining permission to develop a Japanese version, a forward and back translation method was used to develop the CARS-J. The reliability and validity of the CARS-J has been confirmed among Japanese patients with breast cancer, although the factor structure differed slightly to that in the original study. This suggested there were some cross-cultural differences in the construct validity of fear of recurrence[16, 17]. In this study, we assessed overall fear of breast cancer recurrence using four items that covered frequency, potential for upset, consistency, and intensity of fear. The cut-off point for the CARS-J total score used to screen clinical psychological distress was defined as 11, as described elsewhere[18].

Brief Pain Inventory (bpi) And Pain Interference

The BPI has been shown to be a valid and reliable measure for assessing the intensity of postsurgical pain and pain interference in multiple aspects of life[19]. In this study, we used a short version of the BPI that uses a 24-hour recall period for patients developing CPSP. The BPI is a widely used measurement tool for assessing clinical pain and has proven reliability and validity[19–21]. We assessed the average pain severity in the last 24 hours, rated on a scale from 0 to 10. Higher scores indicate worse pain. The BPI pain interference (BPI-PI) subscale consists of seven items that assess enjoyment of life, general activity, walking ability, mood, sleep, normal work, and relationships with other people. Responses are on an 11-point scale from 0 = “no interference” to 10 = “complete interference”[22].

Statistical Analyses

The associations between patient characteristics and the presence of CPSP and the need for CPSP treatment were assessed using Student *t*-, χ^2, and Fisher’s exact probability tests. The association between the presence of CPSP or need for CPSP treatment and overall fear of breast cancer recurrence scores (CARS-J) or pain severity and pain interference scores (BPI, BPI-PI) were assessed by Student *t*-tests. Because a cut-off value for the BPI-PI total score that predicts patients who need treatment for

CPSP has not yet been reported, we performed receiver operating characteristic (ROC) curve analysis to determine the optimal cut-off point for the BPI-PI total score. We used Youden's index (sensitivity + specificity − 1), which corresponded to a point on the ROC curve with the highest vertical distance from the 45° diagonal line.

Univariate and multivariate logistic regression models were developed to predict patients who develop CPSP and those who need treatment for CPSP. Variables included in the univariate logistic regression model were age at surgery, time (months) since surgery, BMI at surgery, use of analgesics within the first month after surgery, type of surgery, axillary lymph node dissection procedure, breast reconstruction, chemotherapy, radiotherapy, presence of family members, and presence of psychiatric disorders. Age at surgery and time since surgery were continuous variables. These factors were determined based on risk factors for CPSP reported in previous studies[5, 6, 11, 23–27]. We also included the distribution of postsurgical pain regions, CARS-J total score, and BPI-PI total score in the univariate analyses, as these factors may affect the presence of CPSP and the need for CPSP treatment. Variables for the multivariate logistic regression model were selected from the variables included in the univariate logistic regression model using a stepwise approach. The model predictive value was assessed with the C-statistic (area under the curve) in the ROC analysis. The level of statistical significance was set at a *P*-value less than 5%. All statistical calculations were performed with R software version 4.0.0 (https://www.R-project.org/).

Results

Nearly half of participating patients developed CPSP after breast cancer surgery

This study included 305 patients after breast cancer surgery who met the eligibility criteria. Among these 305 patients, the current mean age was 52.5 years (range, 32–65 years), the mean age at surgery was 46.9 years (range, 27–63 years), and the mean time since surgery was 67.1 months (range, 12–386 months). We found that 156 patients (51%) reported CPSP after breast cancer surgery. We also found that a shorter time (months) since surgery ($P < 0.001$) and use of analgesics within the first month after surgery ($P < 0.001$) were positively associated with the presence of CPSP. The other variables investigated were not associated with the presence of CPSP (Table 1).

Overall fear of breast cancer recurrence (CARS-J) was significantly associated with the presence of CPSP

The overall fear of breast cancer recurrence was assessed with the CARS-J for all 305 patients. The mean scores for all CARS-J dimensions were significantly higher among patients who developed CPSP than among those who did not develop CPSP (frequency: $P < 0.001$, potential for upset: $P = 0.011$, consistency: $P < 0.001$, intensity of fear: $P < 0.001$, total score: $P < 0.001$) (Table 2). However, among the 156 patients that developed CPSP, only "consistency of fear of recurrence" was significantly higher in patients who needed treatment for CPSP ($P = 0.017$). A high CARS-J total score tended to be positively associated with the need for CPSP treatment, although the difference was not significant, which may attributable to the relatively small sample size. The other CARS-J dimensions were not associated with the need for CPSP treatment (Supplementary Table 1).

Approximately 40% of patients that developed CPSP needed CPSP treatment

Among the 156 patients that developed CPSP, the current mean age was 52.4 years (range, 33–65 years), the mean age at surgery was 47.7 years (range, 27–63 years), and the mean time since surgery was 56.5 months (range, 12–209 months). We found that 61 of these patients (39%) needed treatment for CPSP. We also found that the distribution of ≥ 2 postsurgical pain regions ($P = 0.006$) and the presence of psychiatric disorders ($P = 0.029$) were positively associated with the need for CPSP treatment. The other variables investigated were not associated with the need for CPSP treatment (Table 3).

Pain severity and pain interference was significantly associated with the need for CPSP treatment

Pain severity and pain interference scores were calculated for the 156 patients who developed CPSP. The mean pain severity score in the last 24 hours was higher in patients who needed treatment for CPSP compared with those who did not need treatment for CPSP ($P < 0.0001$) although the difference was relatively small. In addition, the mean and total scores for the BPI-PI dimensions were significantly higher in patients who needed treatment for CPSP compared with those who did not need treatment for CPSP (general activity: $P = 0.031$, mood: $P < 0.0001$, walking ability: $P = 0.040$, normal work: $P < 0.001$, sleep: $P = 0.006$, enjoyment of life: $P = 0.001$, BPI-PI total score: $P < 0.001$). The BPI-PI dimension “relationships with other people” was not significantly associated with the need for CPSP treatment (Table 4).

CARS-J total score ≥ 11 was an independent predictor of the presence of CPSP

We further investigated predictive factors for the presence of CPSP after breast cancer surgery in all 305 patients using logistic regression models. The univariate analyses showed that factors significantly associated with the presence of CPSP were shorter time (months) since surgery ($P = 0.003$), use of analgesics within the first month after surgery ($P < 0.001$), and a CARS-J total score ≥ 11 ($P = 0.001$). Variables included in the multivariate logistic regression model were selected using a stepwise approach (months after surgery, use of analgesics within the first month after surgery, radiotherapy, presence of psychiatric disorders, and CARS-J total score). We found that fewer months after surgery (odds ratio [OR] 0.99, 95% confidence interval [CI]: 0.98–0.99, $P < 0.001$), use of analgesics within the first month after surgery (OR 3.06, 95% CI: 1.76–5.44, $P < 0.001$), and CARS-J total score ≥ 11 (OR 2.22, 95% CI: 1.30–3.81, $P = 0.004$) were independent predictors of the presence of CPSP (Table 5). The predictive value (C-statistic) for this model was 0.73.

CARS-J total score ≥ 11 was also an independent predictor of the need for CPSP treatment after breast cancer surgery

Logistic regression models were also used to examine the predictors of the need for CPSP treatment among the 156 patients who developed CPSP after breast cancer surgery. The cut-off point for the BPI-PI total score as determined by ROC analysis was 4 (area under the curve: 0.75) (Supplementary Figure S1). The univariate analyses showed that the distribution of ≥ 2 postsurgical pain regions ($P = 0.004$), use of analgesics within the first month after surgery ($P = 0.026$), and presence of psychiatric disorders ($P =$

0.026) were significantly associated with the need for CPSP treatment. BPI-PI total score was not associated with the need for CPSP treatment. Multivariate variables in the logistic regression model were selected using a stepwise approach (distribution of postsurgical pain regions, use of analgesics within the first month after surgery, reconstruction, and CARS-J total score). We found that distribution of ≥ 2 postsurgical pain regions (OR 2.52, 95% CI: 1.16–5.57, $P = 0.020$) and CARS-J total score ≥ 11 (OR 2.59, 95% CI: 1.14–6.28, $P = 0.028$) were independent predictors of the need for CPSP treatment (Table 6). The predictive value (C-statistic) for this model was 0.71.

Discussion

The results of this study revealed that nearly half of participating patients developed CPSP after breast cancer surgery and 39% needed treatment for CPSP. We also found that the fear of breast cancer recurrence (as assessed by the CARS-J) and ≥ 2 postsurgical pain regions were independent predictors of the need for treatment for CPSP.

In the present study, we showed that the fear of cancer recurrence as assessed by the CARS-J was an independent predictor of the presence of CPSP. This result was consistent with a previous study that revealed a strong association between postsurgical pain and fear of breast cancer recurrence as assessed by the CARS[13]. In addition, the predictive value (C-statistic) for the logistic model that predicts the presence of CPSP indicated good discriminatory power. These findings suggested that the overall fear of breast cancer recurrence as assessed by CARS-J may help to identify patients who develop CPSP after breast cancer surgery.

The incidence and predictors of CPSP after breast cancer surgery have been reported in several studies[5–7, 11, 23–27]. However, the need for treatment for CPSP has not previously been investigated. Among patients who developed CPSP after breast cancer surgery in this study, we found that 39% needed treatment for pain. Our multivariate analysis also revealed that fear of cancer recurrence (as assessed by the CARS-J) and ≥ 2 postsurgical pain regions were independent predictors of the need for treatment of CPSP. Since the predictive value (C-statistic) for this logistic model indicated good discriminatory power, these clinical factors may help to predict patients at high-risk that need treatment for CPSP early in the postsurgical period. To our knowledge, this is the first report to show the proportion and predictors of patients who need treatment for CPSP after breast cancer surgery.

A previous study reported that the intensity of pain interference as assessed by the BPI was significantly higher in patients with severe CPSP after breast cancer surgery[9]. This study showed that the BPI-PI total score was significantly higher in patients who needed treatment for CPSP; however, it was not an independent predictive factor of the need for CPSP treatment. This apparent discrepancy may partly be attributable to the relatively small number of patients in our sample. In addition, the cut-off point for the BPI-PI total score to predict the need for CPSP treatment was determined for the first time in this study, and should be re-evaluated using a different dataset in a further study.

Our finding that 39% of patients needed treatment for CPSP highlights the need for effective and evidence-based treatments for pain after breast cancer surgery. A variety of approaches to the treatment of CPSP, including presurgical or postsurgical pharmacological managements, have been reported in recent studies[28, 29]. However, standard treatment for CPSP after breast cancer surgery has not yet been established. Recently, psychological interventions were revealed to be effective for alleviating the fear of recurrence among cancer survivors[30]. Since the fear of breast cancer recurrence was strongly associated with the presence of CPSP, we suggest that psychological interventions early in the postsurgical period may reduce the incidence and severity of CPSP. However, further studies are required to validate this hypothesis.

The present study had some limitations. First, this study was conducted at a single institution and included a relatively small number of patients. Second, because our investigation was designed to be cross-sectional and included patients at least 1 year after breast cancer surgery, the present results may not be sufficiently adaptable to predict patients in the early postsurgical period who have CPSP or need treatment for CPSP. Third, the results may not be applicable to patients from other cultures as the variables related to CPSP (e.g., fear of cancer recurrence) investigated in this study appear to be influenced by the patients' cultural background.

In summary, we identified that 39% of patients who develop CPSP after breast cancer surgery need treatment for CPSP and showed that the fear of cancer recurrence (as assessed by the CARS-J) and ≥ 2 postsurgical pain regions were independent predictors of the need for CPSP treatment. We are planning to conduct a further clinical trial to determine whether early postsurgical psychological interventions for patients at high-risk and who need treatment for CPSP are effective in preventing or reducing CPSP after breast cancer surgery.

Declarations

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Conflict of interest

The authors declare no competing interests.

Ethics approval

This study protocol (60-19-0031) was approved by the Institutional Review Board of Nagoya City University Graduate School of Medical Sciences and conforms to the guidelines of the guidelines of the Declaration of Helsinki.

Consent to participate

Written informed consent for this comprehensive research was obtained from all patients involved in this study.

Consent for publication

Not applicable.

Availability of data and material

The datasets analyzed during the present study are available from the corresponding author on reasonable request.

Code availability

Not applicable.

References

1. Sharma R (2019) Breast cancer incidence, mortality and mortality-to-incidence ratio (MIR) are associated with human development, 1990–2016: evidence from Global Burden of Disease Study 2016. Breast Cancer 26:428–445. https://doi.org/10.1007/s12282-018-00941-4
2. Kohler BA, Sherman RL, Howlader N et al (2015) Annual Report to the Nation on the Status of Cancer, 1975–2011, Featuring Incidence of Breast Cancer Subtypes by Race/Ethnicity, Poverty, and State. J Natl Cancer Inst 107:djv048. https://doi.org/10.1093/jnci/djv048
3. de Gelder R, Heijnsdijk EAM, Fracheboud J et al (2015) The effects of population-based mammography screening starting between age 40 and 50 in the presence of adjuvant systemic therapy. Int J cancer 137:165–172. https://doi.org/10.1002/ijc.29364
4. Mehdi S, Abbas H, Al A et al (2019) Health-related quality of life of breast cancer patients in the Eastern Mediterranean region: a systematic review and meta-analysis. Breast Cancer Res Treat 174:585–596. https://doi.org/10.1007/s10549-019-05131-0
5. Andersen KG, Duriaud HM, Jensen HE et al (2015) Predictive factors for the development of persistent pain after breast cancer surgery. Pain 156:2413–2422. https://doi.org/10.1097/j.pain.0000000000000298
6. Okamoto A, Yamasaki M, Yokota I et al (2018) Classification of acute pain trajectory after breast cancer surgery identifies patients at risk for persistent pain: a prospective observational study. J Pain Res 11:2197–2206. https://doi.org/10.2147/JPR.S171680

7. Wang L, Cohen JC, Devasenapathy N et al (2020) Prevalence and intensity of persistent post-surgical pain following breast cancer surgery: a systematic review and meta-analysis of observational studies. Br J Anaesth 125:346–357. https://doi.org/10.1016/j.bja.2020.04.088
8. Mejdahl MK, Andersen KG, Gärtner R et al (2013) Persistent pain and sensory disturbances after treatment for breast cancer: six year nationwide follow-up study. BMJ 346:f1865. https://doi.org/10.1136/bmj.f1865
9. Burckhardt CS, Jones KD (2005) Effects of chronic widespread pain on the health status and quality of life of women after breast cancer surgery. Health Qual Life Outcomes 3:30. https://doi.org/10.1186/1477-7525-3-30
10. Marschner N, Trarbach T, Rauh J et al (2019) Quality of life in pre- and postmenopausal patients with early breast cancer: a comprehensive analysis from the prospective MaLife project. Breast Cancer Res Treat 175:701–712. https://doi.org/10.1007/s10549-019-05197-w
11. Hamood R, Hamood H, Merhasin I, Keinan-Boker L (2018) Chronic pain and other symptoms among breast cancer survivors: prevalence, predictors, and effects on quality of life. Breast Cancer Res Treat 167:157–169. https://doi.org/10.1007/s10549-017-4485-0
12. Akechi T, Okuyama T, Endo C et al (2011) Patient's perceived need and psychological distress and/or quality of life in ambulatory breast cancer patients in Japan. Psychooncology 20:497–505. https://doi.org/10.1002/pon.1757
13. van den Beuken-van Everdingen MHJ, Peters ML, de Rijke JM et al (2008) Concerns of former breast cancer patients about disease recurrence: a validation and prevalence study. Psychooncology 17:1137–1145. https://doi.org/10.1002/pon.1340
14. Mishel MH, Germino BB, Gil KM et al (2005) Benefits from an uncertainty management intervention for African-American and Caucasian older long-term breast cancer survivors. Psychooncology 14:962–978. https://doi.org/10.1002/pon.909
15. Vickberg SMJ (2003) The Concerns About Recurrence Scale (CARS): a systematic measure of women's fears about the possibility of breast cancer recurrence. Ann Behav Med 25:16–24. https://doi.org/10.1207/S15324796ABM2501_03
16. Akechi T, Momino K, Yamashita T et al (2014) Contribution of problem-solving skills to fear of recurrence in breast cancer survivors. Breast Cancer Res Treat 145:205–210. https://doi.org/10.1007/s10549-014-2929-3
17. Momino K, Akechi T, Yamashita T et al (2014) Psychometric properties of the Japanese version of the concerns about recurrence scale (CARS-J). Jpn J Clin Oncol 44:456–462. https://doi.org/10.1093/jjco/hyu032
18. Akechi T, Momino K, Iwata H (2015) Brief screening of patients with distressing fear of recurrence in breast cancer survivors. Breast Cancer Res Treat 153:475–476. https://doi.org/10.1007/s10549-015-3537-6
19. Mendoza TR, Chen C, Brugger A et al (2004) Lessons learned from a multiple-dose post-operative analgesic trial. Pain 109:103–109. https://doi.org/10.1016/j.pain.2004.01.015

20. Cleeland CS, Gonin R, Hatfield AK et al (1994) Pain and its treatment in outpatients with metastatic cancer. N Engl J Med 330:592–596. https://doi.org/10.1056/NEJM199403033300902
21. Cleeland CS, Nakamura Y, Mendoza TR et al (1996) Dimensions of the impact of cancer pain in a four country sample: new information from multidimensional scaling. Pain 67:267–273. https://doi.org/10.1016/0304-3959(96)03131-4
22. Cleeland CS, Ryan KM (1994) Pain assessment: global use of the Brief Pain Inventory. Ann Acad Med Singapore 23:129–138
23. Bruce J, Thornton AJ, Powell R et al (2014) Psychological, surgical, and sociodemographic predictors of pain outcomes after breast cancer surgery: a population-based cohort study. Pain 155:232–243. https://doi.org/10.1016/j.pain.2013.09.028
24. Van Helmond N, Timmerman H, Van Dasselaar NT et al (2017) High body mass index is a potential risk factor for persistent postoperative pain after breast cancer treatment. Pain Physician 20:E661–E671
25. Manfuku M, Nishigami T, Mibu A et al (2019) Comparison of central sensitization-related symptoms and health-related quality of life between breast cancer survivors with and without chronic pain and healthy controls. Breast Cancer 26:758–765. https://doi.org/10.1007/s12282-019-00979-y
26. Roth RS, Qi J, Hamill JB et al (2018) Is chronic postsurgical pain surgery-induced? A study of persistent postoperative pain following breast reconstruction. Breast 37:119–125. https://doi.org/10.1016/j.breast.2017.11.001
27. Wallace MS, Wallace AM, Lee J, Dobke MK (1996) Pain after breast surgery: a survey of 282 women. Pain 66:195–205. https://doi.org/10.1016/0304-3959(96)03064-3
28. Tait RC, Zoberi K, Ferguson M et al (2018) Persistent Post-Mastectomy Pain: Risk Factors and Current Approaches to Treatment. J Pain 19:1367–1383. https://doi.org/10.1016/j.jpain.2018.06.002
29. Reyad RM, Omran AF, Abbas DN et al (2019) The Possible Preventive Role of Pregabalin in Postmastectomy Pain Syndrome: A Double-Blinded Randomized Controlled Trial. J Pain Symptom Manage 57:1–9. https://doi.org/10.1016/j.jpainsymman.2018.10.496
30. Tauber NM, O'Toole MS, Dinkel A et al (2019) Effect of Psychological Intervention on Fear of Cancer Recurrence: A Systematic Review and Meta-Analysis. J Clin Oncol Off J Am Soc Clin Oncol 37:2899–2915. https://doi.org/10.1200/JCO.19.00572

Tables

Due to technical limitations, table 1 to 6 is only available as a download in the Supplemental Files section.

Supplementary Files

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