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## The Unique Mental Impacts of Breast-Conserving Surgery and Mastectomy According to a Multi-Centered Cross Sectional Survey Conducted in Japan

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### ABSTRACT

**Background:** Improving health-related quality of life (HRQOL) has become a fundamental goal of breast cancer management. This study aimed to examine the differences between the QOL outcomes of breast-conserving surgery (BCS) and mastectomy. We also established structural equation models for BCS and mastectomy to elucidate their unique effects on QOL.

**Methods:** Between July 2019 and November 2019, 254 patients, who were scheduled to visit one of four clinics, were recruited for this study. We evaluated HRQOL using various questionnaires, such as the BREAST-Q, EQ-5D-5L, and Hospital Anxiety and Depression Scale (HADS). The relationships among the examined clinical indicators were evaluated using structural equation modeling (SEM).

**Results:** The QOL scores of the BCS group were better than those of the mastectomy group ( $0.85 \pm 0.129$  vs.  $0.81 \pm 0.12$ ,  $P=0.020$ ). Also, anxiety ( $2.94 \pm 2.95$  vs.  $3.81 \pm 3.08$ ,  $P=0.025$ ) and depression ( $2.55 \pm 2.77$  vs.  $3.74 \pm 3.19$ ,  $P=0.002$ ) were less severe in the BCS group than in the mastectomy group. Furthermore, the relationships among QOL status and mental health status were more complex in the BCS group than in the mastectomy group (Chi-square minimization p-value: 0.231 vs. 0.469, respectively). Also, depression directly affected QOL in the mastectomy group ( $R=-0.47$ ), but not in the BCS group.

**Conclusions:** There were differences in QOL and mental health between the BCS and mastectomy groups. SEM is useful for identifying such differences, which can be used to develop strategies for improving QOL.

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### Introduction

Health-related quality of life (HRQOL) has become a fundamental goal of breast cancer management.<sup>1</sup> The mortality rate of breast cancer is decreasing, whereas the incidence rate of breast cancer is on the rise. At present, one in eight women

are diagnosed with breast cancer, and the 5-year survival rate of the disease was reported to be >90%.<sup>2</sup> Thus, the number of breast cancer survivors is increasing. Therefore, determining the patients' QOL status and the factors that affect it are essential for improved decision-making regarding the treatment of breast cancer.

The type of surgical procedure used to treat breast cancer has no impact on survival among patients with early stage cancer.<sup>3, 4</sup> Therefore, breast-conserving surgery (BCS) is preferable to radical mastectomy for early stage breast cancer. On the other hand, it is unclear whether BCS and mastectomy produce different HRQOL outcomes.<sup>5-8</sup> In general, BCS is less invasive than mastectomy, and hence, the postoperative QOL of patients that undergo BCS might be better than that of patients who undergo mastectomy. However, previous studies have reported conflicting results regarding the QOL outcomes of patients that underwent BCS or mastectomy, and the reasons for these discrepancies are unclear.

The BREAST-Q is one of the best measures for assessing the HRQOL of breast cancer patients. It has been validated and translated into thirty different languages.<sup>9, 10</sup> The 5-level EuroQol 5-dimension version (EQ-5D-5L) is also a useful assessment tool for estimating QOL and provides a QOL score, which can be used to calculate quality-adjusted life-year and incremental cost-effectiveness ratio values.<sup>11-14</sup> The Hospital Anxiety and Depression Scale (HADS) is an assessment tool that is commonly used to evaluate mental health status after surgery, including general outpatients.<sup>15, 16</sup> We evaluated QOL from multiple viewpoints because mental status is closely related to QOL in breast cancer patients, and the relationships among QOL indicators are complex.<sup>17</sup> To evaluate QOL in breast cancer patients, we combined the three questionnaires mentioned above and attempted to elucidate the complex relationships between the factors that affect QOL.

Structural equation modeling (SEM) is used to elucidate complex relationships among multiple variables<sup>18</sup> and involves simultaneously solving systems of linear equations. The QOL of breast cancer patients is affected by a complex range of factors, and hence, is difficult to understand. SEM might offer a general structure for assessing the QOL of breast cancer patients and help to visualize the relationships among clinical and social factors.

This study aimed to examine the differences between the QOL outcomes of BCS and mastectomy. Second, we established structural equation models for BCS and mastectomy to elucidate the unique characteristics of these procedures.

## Methods

### *Study subjects*

Between July 2019 and November 2019, 254 patients, who were scheduled to make outpatient visits to one of four clinics, were recruited for this cross-sectional study after providing informed consent. The four clinics were Sapporo Medical University Hospital, Sapporo Breast Surgical Clinic, Higashi-Sapporo Hospital, and Sapporo Kotoni Breast Clinic, which belong to the Sapporo breast medical team union. Patients who had undergone BCS or mastectomy for breast cancer more than three months ago and agreed to respond to the relevant questionnaires were eligible for this study. We recruited as many eligible patients as possible during the study period. The study protocol complied with the Declaration of Helsinki and was approved by the internal review board of Sapporo Medical University (approval ID: 312-68; approval date: July 11, 2019). Informed consent was obtained from all study subjects.

### *Ethical approval*

The procedures in this study complied with the ethical standards of the institutional review board of Sapporo Medical University, Sapporo, Japan (312-68) and the 1964 Declaration of Helsinki and its amendments or comparable ethical standards.

### *Informed consent*

Informed consent was sought from all study participants.

### *BREAST-Q questionnaire*

The BREAST-Q mastectomy module and breast-conserving therapy module (postoperative) each consist of the following 6 domains: BQ1: psychological well-being, BQ2: sexual well-being, BQ3: satisfaction with breasts, BQ4: physical well-being: chest, BQ5: satisfaction with the medical team, and BQ6: adverse effects of radiotherapy.<sup>19</sup> Each domain consists of 4 to 12 items and 3 to 5 scales. The score for each scale is converted to a 100-point scale using a conversion table. Thus, the score for each scale ranges from 0 (very dissatisfied) to 100 (very satisfied). The Japanese BREAST-Q, version 2.0, was used in this study.

### *EQ-5D-5L questionnaire*

The EQ-5D-5L questionnaire,<sup>14</sup> whose Japanese version has been validated in previous studies,<sup>11, 12</sup> was applied in interviews to estimate QOL utility values. The five aspects evaluated by the EQ-5D-5L are mobility (MO), self-care (SC), usual activities (UA), pain/discomfort (PD), and anxiety/depression (AD), each of which has five levels of severity. Level 1 shows that the patient can do the relevant activity without any difficulty or feels comfortable. Level 5 shows the patient performs the relevant activity with difficulty or feels uncomfortable. Using a scoring function developed for Japan, these health status



parameters were changed into utility values from 0 to 1, where 0 indicated death and 1 showed full health. A utility value calculator is available on the EQ-5D homepage (<https://euroqol.org/>), and the coefficients for each of the five dimensions (MO, SC, UA, PD, and AD) are described in the literature.<sup>11</sup> We registered our decision to use the EQ-5D-5L before the patients were recruited (ID: 26966).

#### *Hospital Anxiety and Depression Scale questionnaire in Japanese*

The HADS is a 14-item self-reported questionnaire which evaluates depression (7 items) and anxiety (7 items) over the preceding week.<sup>16</sup> Each item is evaluated on a 4-point Likert Scale (0–3), e.g., “I can laugh and see the funny side of things” (0: most of the time; 3: not at all). Each subscale score is obtained by summing the scores for each item on the subscale (subscale ranges: 0–21), with higher scores indicating greater severity. Following previous research, the mean subscale values were interpreted as follows: 0–7: “normal”, 8–10: “mild”, 11–15: “moderate”, and 16–21: “severe”.<sup>20</sup> The reliability statistic for anxiety and depression was 0.852.

#### *Clinical outcomes of interest*

Physical and pathological data were collected from the questionnaires or the participants’ medical records after providing informed consent. The distributions of each clinical variable are analyzed by Kolmogorov–Smirnov test.

#### *Statistical analysis*

SPSS (version 22, IBM-SPSS, Inc., Armonk, New York, United States) was used to analyze the data. The independent sample t-test was run for comparisons between the groups. We used to Levene’s test assess the equality of variances for each variable in comparisons between the two groups. We performed descriptive statistical analyses and the chi-square test to compare the groups’ demographic data. The results are presented as mean±SD values. P-values of <0.05 are considered to be significant.

#### *Structural equation modeling*

QOL-related variables and clinical variables were used to create structural equation models using the Amos software (IBM SPSS Amos, Version 20.0, IBM-SPSS, Inc., Armonk, New York, United States). SEM is used to estimate theoretical models of the correlations between individual variables within a given population. It can be used to visualize the relationships among variables in order to better understand the overall global situation in specific conditions.<sup>18</sup> Standardized effects with corresponding 95% confidence intervals were measured using the bootstrapping method. In this study, the six subdomains of the BREAST-Q, HADS-anxiety,

HADS-depression, the QOL utility value, and the time since surgery were used to identify the roles of the variables. Model fit was evaluated using the following standards proposed by McDonald and Ho<sup>21</sup>: a good model fit is indicated by a chi-square minimization p-value of >0.05, a comparative fit index (CFI) of >0.95, and a root mean square error of approximation (RMSEA) of <0.05. Over a hundred models were compared, and the one with the smallest Akaike’s Information Criterion (AIC) with a normed fit index (NFI) and a Tucker-Lewis Index (TLI) close to 1.000 was selected. The subscale internal consistency and variance values for single indicator latent variables were specified to reduce the measurement error in the model.

#### **Results**

The clinical backgrounds of the patients are shown in Table 1. A total of 254 patients were recruited for this study after providing written informed consent. There were no differences in the treating institution, body mass index (BMI), age, time since surgery, the incidence of lymphedema, the current management strategy, progesterone receptor (PgR) status, human epidermal growth factor receptor 2 (HER2) status, the Ki-67 index, marital status, child status, housing status, or employment status between the BCS and mastectomy groups. There were significant differences between the groups in the TNM stage ( $P<0.001$ ); the frequencies of reconstruction (1.7% vs. 13.0%,  $P=0.001$ ), axillary lymph node dissection (26.7% vs. 38.4%,  $P=0.049$ ), radiotherapy (68.1% vs. 18.1%), and ER positivity (88.6% vs. 78.5%,  $P=0.034$ ); and economic status ( $P=0.040$ ).

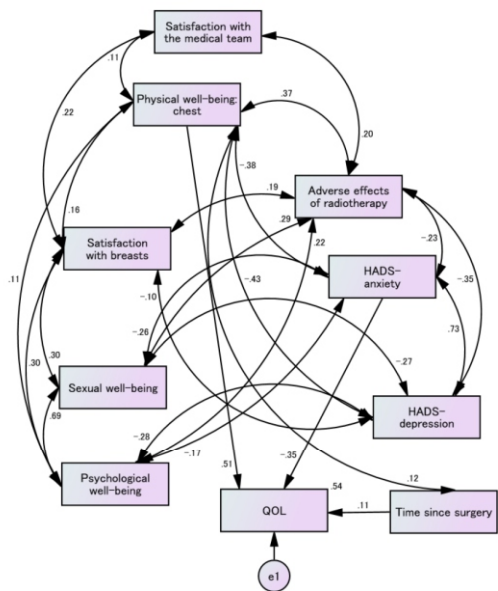
The QOL questionnaire scores are shown in Table 2. The scores for psychological well-being ( $56.9\pm 23.4$  vs.  $46.5\pm 19.1$ ,  $P<0.001$ ), sexual well-being ( $43.4\pm 19.5$  vs.  $25.6\pm 20.3$ ,  $P<0.001$ ), satisfaction with breasts ( $59.7\pm 18.2$  vs.  $41.3\pm 16.6$ ,  $P<0.001$ ), QOL ( $0.8549\pm 0.1279$  vs.  $0.8168\pm 0.1287$ ,  $P=0.020$ ), HADS-anxiety ( $2.94\pm 2.95$  vs.  $3.81\pm 3.08$ ,  $P=0.025$ ), and HADS-depression ( $2.55\pm 2.77$  vs.  $3.74\pm 3.19$ ,  $P=0.002$ ) differed significantly between the groups. On the other hand, the scores for physical well-being (chest), satisfaction with the medical team, and the adverse effects of radiotherapy did not differ significantly between the groups.

SEM of the BCS (Figure 1) and mastectomy (Figure 2) groups were performed. In the BCS group, the following standardized direct effects on QOL were detected: physical well-being (chest): 0.510, HADS-anxiety: -0.350, and time since surgery: 0.11 (Figure 1). The squared multiple correlations coefficient for the relationships among QOL and the factors in the model were 0.541. Some BREAST-Q domains were correlated with each other, and the model was complex (Figure 1), but exhibited very good fit values (CMIN: 0.231, RMSEA: 0.044, CFI:

**Table 1.** Demographic and clinical characteristics of the patients

	Total(N=254)	BCS (N=116)	Mastectomy(N=138)	P-values
Institution(HS:KN:SN:UH)	42:41:45:126	18:21:21:56	24:20:24:70	0.864
BMI(mean±SD)	22.85±3.97	23.13±4.14	22.29±3.55	0.943
Age(years)	55.3±11.7	55.1±12.3	55.5±12.3	0.763
Time since surgery(days)	1329±1345	1163±1236	1665±1495	0.570
TNM stage (0:I:IIA:IIB:IIC:IIIA:IIIB:IIIC)	23:117:62:29:10:5:6:2	13:68:24:10:0:0:1:0	10:29:38:19:10:5:5:2	<0.001
Reconstruction(Y:N)	20:234 (7.9%)	2:114	18:120	0.001
Axial lymph node dissection(Y:N)	84:170 (33.1%)	31:85	53:85	0.049
Lymphedema (Y:N)	19:235 (7.5%)	9:107	10:128	0.877
Radiotherapy(Y:N)	104:150 (40.9%)	79:37	25:113	<0.001
Current management (none:hormone therapy:chemotherapy:radiotherapy)	85:151:16:2 (hormone therapy: 59.4%)	36:74:5:1	49:77:11:1	0.492
ER (Y:N)				
PgR (Y:N)	207:42 (83.1%)	101:13 (88.6%)	106:29 (78.5%)	0.034
HER2 (Y:N)	178:70 (71.8%)	86:28	92:42	0.237
Ki-67	78:170 (52.7%)	30:84	48:86	0.108
Married (Y:N)	18.9±17.1	17.9±15.9	21.1±19.5	0.089
Has children(Y:N)	168:86 (66.1%)	72:44	96:42	0.209
Housing (with others:alone)	167:87 (65.7%)	70:46	97:41	0.096
Employed (Y:N)	196:58 (77.2%)	88:28	108:30	0.650
Economic situation (very poor:poor:normal:wealthy:very wealthy)	150:104 (59.1%) 10:54:166:14:10	74:42 1:19:84:8:4	76:62 9:35:82:6:6	0.159 0.040

BCS: breast-conserving surgery, HS: Higashi-Sapporo Hospital, KN: Sapporo Kotoni Breast Clinic, SN: Sapporo Breast Surgical Clinic, UH: Sapporo Medical University Hospital, BMI: body mass index, Y: yes, N: no, ER: estrogen receptor, PgR: progesterone receptor, HER2: human epidermal growth factor receptor 2



Fit Index	Breast-conserving surgery	Index values
CMIN	Chi-square Minimization P-value	0.231
RMSEA	Root Mean Square Error of Approximation	0.044
CFI	Comparative Fit Index	0.985
AIC	Akaike's Information Criterion	115.139
NFI	Normed Fit Index	0.931
TLI	Tucker-Lewis Index	0.957

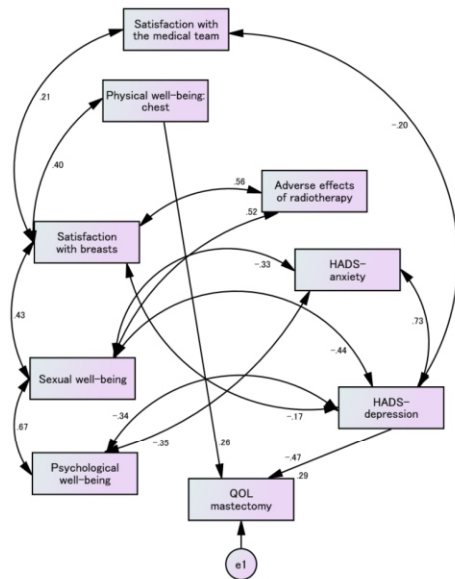
**Figure 1.** Structural equation modeling (SEM) and the fit index of the breast-conserving surgery (BCS).

0.958, AIC: 115.139, NFI: 0.931, and TLI: 0.957). On the other hand, the structural equation model for the patients who underwent mastectomy was more straightforward (Figure 2). There were fewer bidirectional relationships in the mastectomy model than in the BCS model; thus, the correlations among

the factors in the mastectomy model were simpler than those in the BCS model. In the mastectomy group, the following standardized direct effects on QOL were detected: physical well-being (chest): 0.26 and HADS-depression: -0.47 (Figure 2). The squared multiple correlations coefficient for the

**Table 2.** Scores for each questionnaire in the total, breast-conserving surgery, and mastectomy groups

All Patients	Total (N=254)	BCS (N=116)	Mastectomy (N=138)	P-values
Bq1 (N=245, 96.5%)	51.3±21.7	56.9±23.4	46.5±19.1	<0.001
BQ2 (N=122, 48.0%)	33.3±21.8	43.4±19.5	25.6±20.3	<0.001
BQ3 (N=160, 63.0%)	53.6±19.7	59.7±18.2	41.3±16.6	<0.001
BQ4 (N=219, 86.2%)	76.6±18.9	78.4±17.4	74.8±20.2	0.158
BQ5 (N=241, 94.9%)	87.1±17.4	88.8±14.1	85.7±19.8	0.159
BQ6 (N=126, 49.6%)	77.6±22.6	77.2±21.9	79.0±25.5	0.712
QOL (N=250, 98.4%)	0.83±0.12	0.8549±0.1279	0.8168±0.1287	0.020
HADS-anxiety (N=247, 97.2%)	3.41±3.05	2.94±2.95	3.81±3.08	0.025
HADS-depression (N=247, 97.2%)	3.19±3.06	2.55±2.77	3.74±3.19	0.002

**Figure 2.** Structural equation modeling (SEM) and the fit index of the mastectomy.

Fit Index	Mastectomy	Index values
CMIN	Chi-square Minimization P-value	0.469
RMSEA	Root Mean Square Error of Approximation	<0.001
CFI	Comparative Fit Index	1.000
AIC	Akaike's Information Criterion	86.834
NFI	Normed Fit Index	0.928
TLI	Tucker-Lewis Index	1.001

relationships among QOL and the factors in the model were 0.290. The model also displayed very good fit values (CMIN: 0.469, RMSEA: <0.001, CFI: 1.000, AIC: 86.834, NFI: 0.928, and TLI: 1.001).

### Discussion

We investigated HRQOL using the BREAST-Q, EQ-5D-5L, and HADS in 254 breast cancer patients and revealed the relationships that affect the QOL of breast cancer patients treated with mastectomy or BCS. We found that the QOL outcomes of the BCS group were better than those of the mastectomy group. Also, the BCS group exhibited less severe anxiety and depression than the mastectomy group. On the other hand, the relationships between QOL status and mental status were more complex in the BCS group than in the mastectomy group. Our study indicates the importance of intervening to ameliorate anxiety in patients who undergo BCS and depression in patients who undergo mastectomy. The absolute values obtained from the questionnaires could aid the development of future study protocols.

Eltahir et al. compared BREAST-Q scores between patients who underwent mastectomy alone

and those who underwent reconstruction after mastectomy, and their results were quite similar to those obtained in the present study.<sup>22</sup> In the current study, the scores for psychosocial well-being, sexual well-being, and satisfaction with breasts differed significantly between the groups, although breast reconstruction did not affect the BREAST-Q or QOL utility score (data not shown). However, the absolute values for each BREAST-Q subdomain were markedly lower in the present study than in the previous study, which included patients that underwent prophylactic mastectomy, some of whom might not have had cancer. As the present study demonstrated that anxiety and depression affected the QOL of breast cancer patients both directly and indirectly, it is reasonable that our QOL values were lower than those seen in the previous study, as our subjects might have been worried about future life-threatening cancer progression or recurrence.

In the current study, the breast reconstruction rate was only 7.9%, whereas it was 67.2% in the study conducted by Eltahir et al.<sup>22</sup> The low reconstruction rate seen in the present study might have been due to the fact that our study population was composed of Japanese women. Sim et al. reported various breast

reconstruction rates, ranging from 7.6% to 60.0%, for different ethnicities.<sup>23</sup> Lagendijk et al. reported that breast reconstruction improved the QOL of breast cancer patients after surgery.<sup>24</sup> However, we did not observe any improvement in QOL after breast reconstruction (data not shown), except in the satisfaction with breasts subdomain ( $P=0.046$ ). Similarly, a Polish study failed to demonstrate that reconstruction had a QOL advantage over BCS.<sup>25</sup> The impact of breast reconstruction on QOL might depend on ethnic factors, such as race and religion. We need to investigate whether breast reconstruction improves QOL under our specific circumstances.

We found that ER-positive breast cancer was significantly more common in the BCS group than in the mastectomy group (88.6% vs. 78.5%,  $P=0.034$ ). One possible reason for this is that the ER-positive patients in the BCS group achieved better survival outcomes than the ER-negative patients. Furthermore, the ER-negative patients in the mastectomy group had more advanced cancer than those in the BCS group (Table 1;  $P<0.001$ ). Another possible reason is that hormone status affected decisions regarding treatment. We could not reach a definitive conclusion about this due to the study's cross-sectional nature, although hormone status might be associated with QOL and other indicators.

On the other hand, we also found that the ER-positive rate was higher than the PgR-positive rate in this study. Basic research has demonstrated that ER-dependent pathways induce PgR expression.<sup>26</sup> Therefore, theoretically, the ER-positive rate should always be higher than the PgR-positive rate, and the pathological information obtained in this study fit this theory.

Versions of the EQ-5D-5L tariff in various languages have been developed and validated.<sup>11, 27</sup> However, the problem with this tariff is that it involves discontinuous scores with a gap between 1.000 and 0.900, especially in the Japanese and Korean versions.<sup>27,28</sup> Therefore, the QOL scores produced by the EQ-5D-5L could be underestimated in patients with slight health problems. However, different studies, including our study, have produced quite similar values,<sup>24,27</sup> which demonstrates that the EQ-5D-5L exhibits excellent reproducibility. The greatest advantage of the EQ-5D-5L is that it involves a simple questionnaire containing only five questions, which does not take a long time to complete.

The HRQOL of breast cancer patients might alter after surgery, depending on the type of surgery performed, the QOL domains examined, or the time to the QOL evaluation.<sup>7, 29</sup> Our structural equation model for all patients was complicated, which indicated that QOL after breast surgery is influenced by various factors. On the other hand, the structural equation model for the mastectomy group was simpler, but did not exhibit reduced "goodness of

fit". Our findings clearly indicate that QOL models for breast cancer patients need to be specific to BCS or mastectomy. Fehlaue et al. also reported that the HRQOL of breast cancer patients is affected by a complex range of factors, including age, physical functions, and psychological well-being.<sup>30</sup> Our study suggested that the QOL of breast cancer patients should be divided according to the type of surgical procedure performed.

SEM is a multivariate statistical framework, which can be used to reveal the complex relationships among factors.<sup>18</sup> We created various models and selected the one that exhibited the best fit. Huang et al. stated that preoperative communication with patients who undergo BCS regarding the advantages and disadvantages of using SEM is important.<sup>31</sup> Our findings supported their conclusion that patients who undergo BCS need support to ameliorate their anxiety to improve their QOL. However, in these patients, the effects of chest-related physical well-being were more marked than those of anxiety. Our structural equation model indicated that physical support could have a positive impact on the QOL of patients that undergo BCS. On the other hand, depression had a strong direct effect on QOL in the mastectomy group. As depression was correlated with anxiety in the mastectomy group, medication or consultations with mental health specialists could help to improve the QOL of patients that undergo mastectomy.<sup>32</sup>

The main limitation of this study was that due to its cross-sectional nature, we were unable to determine the exact relationships between clinical outcomes and their causes. Although most of the data had a normal distribution, it could not be proven whether the study population accurately represented the parent set. Furthermore, the results obtained for the Japanese population might not be generalizable to breast cancer patients from other geographic areas.

In conclusion, QOL and mental health differed between breast cancer patient that underwent BCS and those who underwent mastectomy. SEM is useful for identifying differences between patients who undergo BCS and those who undergo mastectomy. The management of anxiety is important for supporting patients who undergo BCS. On the other hand, managing depression is important for supporting patients who undergo mastectomy. This study provides some fundamental information that will aid the planning of future studies.

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### Conflicts of interest

The authors declare that they have no conflicts of interest.

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