

QUALITY OF LIFE AND DEPRESSION AMONG FEMALE PATIENTS UNDERGOING SURGICAL TREATMENT FOR BREAST CANCER: A PROSPECTIVE STUDY

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SUMMARY

Background: Breast carcinoma is the most common malignant disease in women in the majority of developed countries. The development of depression as well as the quality of life (QoL) in these patients depends not only on the result of oncologic treatment, but on the cosmetic outcome as well. The primary aim of this prospective study was to investigate the changes in QoL and depressive symptoms among patients undergoing surgical treatment for breast cancer.

Subjects and methods: We conducted a prospective study that included 100 female patients (mean age 60.26 years) who underwent surgical and oncological treatment for breast carcinoma at the University Hospital Center Zagreb, Croatia. The patients were photographed before and after treatment and were required to fill out a standardized quality of life questionnaires QLQ – C30 and QLQ – BR23, Beck Depression Inventory (BDI) and a questionnaire on breast asymmetry.

Results: Our results show that patients had significantly higher QoL levels compared with their pre-surgical results. Statistical trend of a lower degree of depression was also observed. A worse cosmetic outcome (i.e., postoperative asymmetry) was associated with a lower QoL, but there was no association with depression. Depression was significantly related to the level of pain and lower financial status.

Conclusion: QoL improved after surgical treatment of breast cancer and was dependant on postoperative asymmetry, whereas the findings for depressive symptoms remained less clear. Future research should investigate more factors that may contribute to the QoL and degree of depression in this patient population.

Key words: breast surgery - breast cancer - breast asymmetry – depression - quality of life

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INTRODUCTION

Breast cancer is the most common malignancy in females in Croatia and in most of the western countries as well (Ferlay et al. 2012). During 2013, there were 2557 new cases of breast cancer reported in Croatia (Registar za rak Republike Hrvatske 2013). The treatment for breast cancer consists of surgery and adjuvant therapy. Due to cancer prevention measures such as regular examinations by the general practitioner and mammography screenings, this disease is usually diagnosed in the early stages and requires only a lumpectomy in the majority of cases (Veronesi et al. 1990). This surgical technique preserves the breast contour and avoids the need for more radical procedures such as radical mastectomy. Following a lumpectomy, postoperative radiation treatment is always applied (Fisger et al. 2002). Since Veronesi began with breast conserving surgery in patients with diagnosed breast cancer, numerous studies have confirmed the equal oncological value of this type of surgery compared with a classic mastectomy (Veronesi & Zurrida 2007). Although this type of surgery is minimally destructive, our experience as well as experience of other authors has shown that the cosmetic result is not always

satisfactory (Stanton et al. 2001, Medina – Franco et al. 2013) Due to this, many authors have researched the influence of the cosmetic result after breast conserving therapy and observed important factors such as post-operative complications, tumor location and volume of excised tissue (tumor removal) versus breast volume (Cardoso et al. 2007). Jennifer F Waljee found that factors that contribute to breast asymmetry after surgery include younger patient age, increased BMI, larger tumor size and tumor location (upper medial and upper lateral quadrants). They also found that breast asymmetry or overall cosmetic results are dependant on the need for re-excisional surgery, postoperative seroma formation and radiotherapy (Waljee et al. 2008). Cochrane showed in his research that the maximal percentage of breast volume that can be removed without changes in the final cosmetic result is 10% (Cochrane et al. 2003). Surgery and radiotherapy influence the shape and form of the patient's breast, the quality of the skin and subcutaneous tissue and the appearance of the scar (D'Aniello et al. 1999).

In the last two decades, many research papers compared the cosmetic result, quality of life and psychosocial changes related to the type of surgical treatment conducted (Curran et al. 1998, Sheppard & Ely 2008,

Nano et al. 2005, Waljee et al. 2008a, Waljee et al. 2008b). That studies have shown that a poorer cosmetic result generally leads to a lower quality of life and higher levels of depression. In that studies authors just observed the result after the oncologic treatment. There were no investigation that would show the difference before and after surgery and oncologic treatment.

In this prospective study, we specifically focused on the relationship between quality of life and the occurrence of depression in relation to the cosmetic result by using the asymmetry test. The goals of this study were to determine the cosmetic result of breast lumpectomies following surgical and oncologic treatment and to evaluate the level of depression and the quality of life in patients before and after breast cancer treatment. Also we planned to discover if there is relationship between quality of life level, degree of depression and level of asymmetry following treatment.

SUBJECTS AND METHODS

Subjects

This study included 100 female patients who were surgically and oncologically treated at the University Hospital Centre Zagreb, Croatia. Surgical treatment included only a primary breast lumpectomy (the patients had no previous or additional surgical therapy). The study excluded patients with a history of psychiatric illness or those using psychotropic medications. Also, patients who refused adjuvant oncological treatment, patients who underwent other forms of treatment in other medical centers and patients who refused to participate in the study were not included. This research was approved by the Ethics Committee at the University Hospital and School of Medicine, University of Zagreb, Croatia. A consent form was given and signed by all patients who participated in the study.

The average age of the sample group was 60.26 years. The youngest patient was 29 and the oldest 69 years. Most patients were retired (59%), a third of them employed, and the rest were unemployed. Seventy-one percent (71%) of women were married or in a relationship, 12% divorced, 16% widowed, and 1 patient had never married.

Methods

The questionnaires used included the quality of life QLQ - C30, QLQ - BR23, Beck Depression Inventory (BDI) and asymmetry questionnaire taken from BCTOS and modified by Waljee and associates (Waljee and al. 2008a). Patients were asked to complete these questionnaires preoperatively and after completing oncologic treatment.

Their quality of life was assessed by patient responses to 2 generic cancer questionnaires: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire version 3 (EORT QLQ-C30) and

the Breast Cancer-Specific Quality of Life Questionnaire (QLQ BR-23) (Aaronson et al. 1993, Sprangers et al. 1996, Fayers et al. 2001). The QLQ-C30 contains 30 questions and has been grouped into three scales: one global QOL scale (2 questions), five function scales (15 questions) and nine symptom scales (13 questions). Scale scores are the average of responses and can be transformed linearly in a range from 0–100 (as described in the User's Guide) (de Haes et al. 1999) or can be used as raw results. The QLQ-BR23 is comprised of 23 questions and has been grouped into two scales: four function scales (13 questions) and four symptom scales (8 questions). Scale scores can be transformed linearly in a range from 0–100 or used as raw results. For both quality of life questionnaires (QLQ-C30 and QLQ-BR23) function scales and the global QOL scale, a higher score corresponds to a better QOL. For the symptom scales, a higher score indicates more frequent and/or intense symptom experience and thus a lower QOL (King 1996).

The Beck Depression Inventory (BDI) is a questionnaire that is used for the evaluation of the presence and intensity of depression (Beck et al. 1984). The scale consists of 21 symptoms and the patient has to choose the one that best describes their state in the indicated time period. The following criteria is used for measuring the intensity of depression: 0–4 no depression; 5–7 mild depression; 8–15 moderate depression; over 16 points severe depression.

BDI has been successfully used in a number of clinical studies of depression in the general population and in studies of depression in chronic somatic patients (Beck et al. 1997, Steer et al. 1999, Tyralla et al. 2015, Uglešić et al. 2015).

Cosmetic outcome after surgery was assessed by the patient's response to eight questions from the Breast Cancer Treatment and Outcomes Survey (Stanton et al. 2001). Patients were also asked to rate the differences in breast skin color using the same scale modification made by Waljee et al. (Waljee et al. 2008). Answers to each question were rated on a 4 point scale (1 - no difference between breasts, 2 - slight difference between breasts, 3 - moderate difference between breasts, and 4 - large difference between breasts). The responses were normally distributed and averaged to generate an overall asymmetry score. For ease of reporting, response scores were categorized into three groups: minimal asymmetry (scores <15), moderate asymmetry (scores of 15 to 20), and pronounced asymmetry scores >20) (Deutsch & Flickinger 2003, Taylor et al. 1995, Fedoric et al. 2006, Cardoso et al. 2007). Due to sample size issues, we merged the moderate and pronounced asymmetry categories for the purposes of statistical analyses.

Statistical Analysis

Statistical analysis was performed using the SPSS software package, version 20 for Windows operating system. The following parameters of descriptive sta-

tistics were calculated: frequency, proportions, percentages, average values and the corresponding standard deviations. The reliability of the instruments is calculated using the coefficient of internal consistency (Cronbach alpha coefficient). The normality of distribution of the results obtained was verified using the Kolmogorov-Smirnov test. Nonparametric statistics used included Wilcoxon matched pairs test. Parametric analysis of the results included a t-test for dependent and independent samples. The initial level of significance was determined to be an error probability of less than 5% ($p < 0.05$). We used the Bonferroni's adjustment for the p value when comparing multiple QoL dimensions before and after surgery.

RESULTS

Features of the tumor: 98% of patients had an invasive carcinoma while 2% had ductal carcinoma in situ. In 53 women, the tumor was located in the right breast, and in the other 47 women in the left. In all patients the appropriate adjuvant chemotherapy was given. The average tumor size was 18.67 mm. The smallest tumor was 5 mm and the largest was 48 mm. 55% of patients had a tumor in the outer upper quadrant, 17% in the outer lower quadrant, 14% in the lower inner quadrant, 13% in the inner upper quadrant and 1% in the central quadrant.

The average score on the asymmetry questionnaire was 13.24 (SD=3.726), but the most frequent score was 9 (distribution is positively skewed), which means that the majority of women see their breast as minimally asymmetric. More specifically, seventy-six percent (76%) of women reported minimal asymmetry, 19% reported moderate asymmetry, and 5% reported significant breast asymmetry.

The average score on the Beck Depression Inventory before surgery was 10.122 (SD=7.248) - moderate depression, but after the operation it was 8.61 (SD=4.930) - minimal depression. The difference in the depression before and after surgery was not statistically significant (Wilcoxon matched pairs test: $z=1.887$; $p=0.059$), but the border significance level analysis suggests a statistical trend in terms of lower levels of depression after surgery.

The overall quality of life before surgery was 4.46 and after the end of treatment was 5.01. After surgery, the patient's quality of life was better than before surgery. The difference in the result before and after surgery was statistically significant (paired-samples t-test: $t=3.491$, $df=99$, $p=0.001$). Detailed description of the quality of life factors and results can be found in Tables 1 and 2.

As seen in Tables 1 and 2, the following QoL dimensions improved after breast surgery: global QoL, physical, role, cognitive and sexual functioning. On the other hand, levels of fatigue, pain, dyspnoea, and arm symptoms increased. Also patients found that future perspective worse after surgery and oncologic treatment.

We did not find a statistically significant association between the cosmetic result of conservative breast cancer treatment (i.e., minimal and moderate/significant asymmetry categories) with results on the Beck Depression Inventory (independent samples t-test: $t=1.450$, $df=98$, $p=0.150$).

24% of the patients who reported moderate or significant breast asymmetry had worse result on global health status in QLQ-C30 questionnaire comparing the rest of patients (Spearman $\rho=-0.235$, $p=0.019$).

29% of patients after completing their treatment often or almost always felt pain. These patients exhibit a higher level of depression (independent samples t-test: $t=3.885$, $df=98$, $p=0.000$).

16 % of patients who had financial problems were found to be more depressive than those without, and this was found to be statistically significant ($t=20.096$, $df=98$, $p=0.039$).

Study showed that group of patients with moderate and significant asymmetry compared to patient with minimal asymmetry have better role functioning ($U=1177,500$; $p=0.024$) and better cognitive functioning ($U=1172,000$; $p=0.029$). Also sexual functioning is better in a group with moderate and significant asymmetry ($U=1156,500$; $p=0.038$).

DISCUSSION

In this research, we focused on the cosmetic surgical outcome and the patients' quality of life and level of depression before and after breast surgery, as well as on the relationship between breast asymmetry and the quality of life and level of depression.

76% of the patients reported the presence of minor asymmetry following breast surgery, 19% reported moderate asymmetry while 5% reported a high degree of asymmetry. These results support the findings made by Medina-Franco et al. (2013). The patients in their study reported some degree of asymmetry in 27% of patients who underwent breast surgery. One factor which correlated with a higher degree of reported asymmetry was the patient's level of education. Patients with higher degrees of education reported higher levels of breast asymmetry that suggests that this population is more self critical or possesses a higher expectation standard (Medina-Franco et al. 2013). In our study, we did not find a correlation between asymmetry score and level of education.

Similar results were described by Taylor et al. who found that in 82% of cases, patients were satisfied with postoperative breast conserving surgery results (Taylor et al. 1995).

The patients were moderately depressed before surgery while after surgery they improved and reported minimal depressive symptoms. Although statistically significant at a trend level, this can be described by the fact that the survey was initially filled out by the patients soon after they were diagnosed with breast cancer.

Table 1. Differences in multiple quality of life dimensions (QLQ C30) before and after breast surgery

QoL dimensions	Before Surgery	After Surgery	t-test	p
Global health status	4.4600	5.0100	3.491	<i>0.001</i>
Physical functioning	1.4280	1.7140	5.835	<i>0.000</i>
Role functioning	1.3200	1.5400	3.591	<i>0.001</i>
Emotional functioning	1.9575	1.7400	2.843	0.005
Cognitive functioning	1.4200	1.6300	3.045	<i>0.003</i>
Social functioning	1.3150	1.4400	2.082	0.040
Fatigue	1.8100	2.0967	3.989	<i>0.000</i>
Nausea and vomiting	1.1550	1.1600	0.159	0.874
Pain	1.5050	1.8600	5.064	<i>0.000</i>
Dyspnoea	1.6700	1.9600	3.214	<i>0.002</i>
Insomnia	1.8800	2.0600	2.018	0.046
Appetite loss	1.4900	1.5500	0.726	0.470
Constipation	1.3200	1.4100	1.264	0.209
Diarrhoea	1.2300	1.1500	1.378	0.171
Financial difficulties	1.3900	1.6200	2.416	0.018

Bonferroni's adjustment for multiple comparisons reduced the significance level to $p=0.003$. Statistically significant values are highlighted in *italics*

Table 2. Differences in multiple quality of life dimensions (QLQ - BR23) before and after breast surgery

	Before Surgery	After Surgery	t-test	Significance (p)
Body image	1.4000	1.5350	1.969	0.052
Sexual functioning	1.5800	1.8250	3.707	<i>0.000</i>
Sexual enjoyment	1.1200	1.3600	1.886	0.062
Future perspective	2.6300	2.2600	3.489	<i>0.001</i>
Systematic therapy side effects	1.5900	1.5171	1.623	0.108
Breast symptoms	1.3325	1.4275	2.076	<i>0.040</i>
Arm symptoms	1.4967	1.7933	4.804	0.000
Upset by hair loss	0.4500	0.4200	0.283	0.777

Bonferroni's adjustment for multiple comparisons reduced the significance level to $p=0.006$. Statistically significant values are highlighted in *italics*

The difference in depression levels between the patients with minimal and those with moderate of severe breast asymmetry was found to be statistically insignificant. Maybe the explanation to this fact lies in QLQ C30 questionnaire whose results considering body image shows no statistical difference in body image before and after operation. Unlike our research, Waljee (Waljee et al. 2008a,b) found that worse asymmetric results correlated with higher rates of depression.

In our study, there was a positive correlation between depression and postoperative pain, as well as with financial problems following the operation. Perhaps, the former is the reason for the lack of correlation between depression and asymmetry/cosmetic result; patients could be more focused on pain and existential issues rather than personal appearance. Waljee et. al in their study did not comment on these parameters (Waljee et al. 2008a,b).

In Croatia, patients are granted full sick-leave (absence from work), during their complete surgical and oncological treatment. This sometimes requires 6-12 months and during this period, their monthly income is lower than if they were working. This could maybe be the reason that introduces existential obstacles, lowers

the patients' quality of life and could lead to the development of depression.

Caffo reported symptoms of postoperative pain in 33% of patients which correlated with a lower quality of life score in this population (Caffo et al. 2003). As well as the trend for a lower quality of life in patients with a higher degree of postoperative pain, we also found an increase in depressive symptoms in this population as well. Other studies showed that significant number of patients with chronic pain also develops a chronic pain syndrome, which is manifested in intense pain, suffering, pronounced changes in behavior, decreased activity, sleep disorder, anxiety, depression, suicidal ideas, social withdrawal, irritability, fatigue, cognitive difficulties, impaired sexual activities, hopelessness, helplessness and avoiding behavior. Numerous studies support the thesis that pain causes depression because of the current depressive episode which starts after the beginning of pain (Braš et al. 2010).

This study showed that the patient's overall quality of life is correlated with the level of asymmetry. A higher asymmetry score was found to be associated with better cognitive functioning and better sexual functioning.

Although these results at first seem illogical, we can describe this observation as a method at which patients with a worse cosmetic outcome attempt to compensate for their appearance by "keeping busy" with multiple tasks, increasing their cognitive function, and sexual desire. After operation physical, cognitive, social and role functioning is better. It is hard to explain that physical functioning is better although patients feel pain, arm symptoms, breast symptoms are more tired and complain on dyspnea. Maybe just the fact that they are operated and cancer is removed together with better cognitive function gives them push them to start normal functioning compared to period just before operation.

Our study was orientated to investigate an important dilemma that health professionals face daily; can surgeons, oncologists and other hospital personnel recognize which patients are at an increased risk of developing negative psychological symptoms after being diagnosed and operated with breast cancer.

The factors and elements observed in this study can be used postoperatively as a method of detecting and recognizing groups of patients who are at an increased risk of developing depressive symptoms as a consequence of poor cosmetic outcome or a deteriorated quality of life. These patients could be referred to a psychologist or psychiatrist prior to developing depressive symptoms which will undoubtedly influence their treatment and overall quality of life in a positive manner.

CONCLUSION

QoL improved after surgical treatment of breast cancer and was negatively associated with postoperative asymmetry. The findings for depressive symptoms remained less clear (i.e., reduction in depression levels following surgery was significant at a trend level, while there was no association between depression and breast asymmetry). However, depression was significantly related to the level of postoperative pain and lower financial status. Future research should observe more factors that may influence and contribute to the quality of life and the degree of depression in this patient population.

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Contribution of individual authors:

Anto Dujmović: design of the study, literature searches and analyses, statistical analyses, interpretation of data;

Darko Marčinko: design of study, interpretation of data;

Krešimir Bulić: statistical analyses, literature searches;

Hrvoje Kisić: data collecting, literature searches;

Mladen Duduković: data collecting, literature searches;

Davor Mijatović: design of study, interpretation of data.

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