CHAPTER 5 PSYCHOLOGICAL DISTRESS AFTER COMPLETION OF IMPLANT OR DIEP FLAP BREAST RECONSTRUCTION AND THE IMPACT OF POSTOPERATIVE COMPLICATIONS: A PROSPECTIVE FOLLOW-UP STUDY

Submitted

Gopie JP, Tibben A, Brinkman JN, Seynaeve C, Menke-Pluijmers MBE, ter Kuile MM, Timman R, Mureau MAM

Abstract

Background Many studies investigated psychosocial outcomes after breast reconstruction (BR) following mastectomy for breast cancer, however, studies regarding the impact of complications and subsequent surgery on psychological distress (PD) are scarce. The present prospective follow-up study aimed at investigating the effect of complications following BR on psychological distress after completion of the entire BR process.

Methods Patients were approached between December 2007 and May 2010. In total, 196 women awaiting BR were invited for the study of which 152 consented to participate (71 implant BR; 81 DIEP flap BR). Psychological questionnaires with known psychometric properties regarding anxiety, depression and cancer distress, were completed before BR (T0, *n*=145), after one month (T1, *n*=139) and after completion of the entire BR process, approximately 21 months after initial surgery (T2, *n*=119). Complications and subsequent surgery up to T2 were self-reported and obtained from the medical records. Complications, consequent surgery and complete failure of BR were investigated as predictors of PD.

Results All PD outcomes declined to normal levels after BR at T2. Complications and subsequent surgery did not lead to increased PD at T2, but complete failure of BR was related to temporarily higher depression levels at T1 and overall higher cancer distress.

Conclusions All PD outcomes declined to normal levels after BR at T2. Only complete failure of BR was related to overall higher cancer distress and increased depression on the short term. Women with a complete failure of BR should be carefully monitored after surgery regarding their psychological wellbeing.

Introduction

Breast reconstruction (BR) after mastectomy for breast cancer is intended to improve body image, however, there is a considerable risk for complications which may lead to adverse psychological effects [1-4]. Identification of risk factors for psychological distress after BR, including complications and consequent surgery, provides the opportunity to identify patients at increased risk for postoperative distress. Consequently, adequate support can be offered, in addition to routine medical care.

Although several studies investigated the psychosocial impact of BR after mastectomy, only few, mostly retrospective studies focused on the impact of complications on psychological distress [5-8]. One retrospective quantitative study included a short-term follow up period of only three months, showing that psychological distress levels were similar for women with and without complications [7]. Two qualitative studies with very small samples (*n*=6, and *n*=21) found that women were unprepared for the BR process, that they felt it was burdensome physically as well as emotionally, and that the additional operations and the long recovery period were disappointing and unexpected [5;8].

In our previous prospective study we found that women with complications after BR reported significantly higher levels of psychological distress one month after surgery [6]. The present prospective follow-up study aimed at investigating the effect of complications following BR on psychological distress after completion of the entire BR process. We hypothesized that the occurrence of complications, subsequent surgery, and a complete failure of BR would predict more psychological distress on the longer term [5;9-11].

Patients and Methods

Patients

The current investigation is part of a multi-centre prospective follow-up study regarding the psychosocial impact of BR after either prophylactic or therapeutic mastectomy [6;12-15]. Participants for the current study were women who had opted for BR after mastectomy for breast cancer with either an implant or a DIEP flap. Exclusion criteria were: previous BR, detection of recurrent breast cancer either before or during follow-up, and not being able to understand and speak the Dutch language. Women who did not consent or did not react to the primary and reminder invitation were considered non-respondents.

Patients were approached between December 2007 and May 2010 at the Leiden University Medical Center (LUMC), Erasmus University Medical Center, including Daniel den Hoed Cancer Center, Rotterdam, Haga Teaching Hospital the Hague, Rijnland Hospital Leiderdorp, Lange Land Hospital Zoetermeer, Admiral the Ruyter Hospital (Goes, Vlissingen), and Hospital Zorgsaam Terneuzen, the Netherlands. Ethics approval was obtained from all participating hospitals. In total, 196 women awaiting BR were invited for the study (96 implant BR; 100 DIEP flap BR) of which 152 consented to participate (71 implant BR; 81 DIEP flap BR).

Procedure

Before surgery, an invitation letter explaining the procedure and purpose of the study, an informed consent, and a prepaid envelope were sent to all women on the BR waiting lists of the participating hospitals. Patients who consented to participate received a questionnaire including a range of demographic, clinical and psychosocial items which they were requested to fill in before BR (T0). Similar questionnaires were asked to fill in one month after surgery (T1), and at the end of the entire BR procedure (T2). Additional questions at T2 concerned complications and subsequent surgery.

Questionnaires

Dependent variables

The term "psychological distress" (PD) is used as a general term in this paper covering the concepts anxiety, depression and cancer distress.

Anxiety and depression. Anxiety and depressive symptoms were measured with the Hospital Anxiety and Depression Scale (HADS) [16]. The HADS consists of 14 items which are rated on a 4-point Likert scale and includes two subscales, measuring anxiety and depression (both 7 items). Both subscale scores range from 0 to 21. A score of 8 or above can be used as a borderline of clinical significance [16;17]. Good reliability and validity have been reported for the HADS [17;18].

Breast cancer specific distress. Cancer-specific distress regarding breast cancer was measured using the Impact of Event Scale (IES) [19;20]. The IES consists of 15 items which are rated on a 4-point Likert scale. The total IES score (range 0-75) measures the extent to which one is overwhelmed by intrusive thoughts and avoidant behavior regarding a specific traumatic event, in this case 'breast cancer'. A cut-off score of 20 or more can be used as an indication for high symptom levels [21]. Reported reliability and validity of the IES are satisfactory [19;22].

Patient satisfaction. At T2 overall patient satisfaction with aesthetic outcome was rated on a 10-point scale as used in a previous study, ranging from 1 (extremely dissatisfied) to 10 (extremely satisfied) [23].

Independent variables

Baseline characteristics. At T0, baseline characteristics, including demographic and clinical information (e.g., age, having a partner or children, educational level, body mass index (BMI), previous breast cancer, adjuvant therapy, type of BR) were assessed using self-report questionnaires.

Postoperative complications and subsequent surgery. At T2, the occurrence of complications, subsequent surgery and complete failure of BR were reported by the patients. In addition, the occurrence of postoperative complications and subsequent surgery up to T2 (after

completion of the entire BR process) were obtained from the medical records (JPG, MAMM, JNB). A complication was defined as any adverse physical event specifically related to BR occurring until the T2 assessment. A complication was defined as "major" if it had lead to additional surgery, not including aesthetic improvements or the exchange of tissue expanders with implants. Furthermore, complete failure of BR was defined as loss of a tissue expander, implant or total flap which had not been salvaged by a new BR within the current study period.

Statistical analyses

For all patients demographic and clinical information was collected. Missing items from a subscale were inferred by using the mean of the remaining items, if at least 70% of all items had been completed.

Descriptive statistics were calculated for all variables. Baseline differences between participants and women lost to follow-up were analyzed using Chi-square tests, Mann-Whitney U tests, and Student's t-tests.

Complications, subsequent surgery and complete failure of BR obtained from the medical files, were compared with the patient-reported outcomes to check discrepancies using Fisher's exact tests. For the statistical analyses, the occurrence of one or more complications (yes/no) and subsequent surgery (yes/no), number of re-operations (numerical), and complete failure of BR (yes/no) obtained from the medical files were used.

To investigate changes in time in anxiety, depression and cancer distress, multi-level regression analyses (MLA) were performed, which can efficiently handle incomplete time-series data with a minimal loss of information. It corrects for bias when absence of data is dependent on characteristics that are present in the models [24].

First, saturated models were postulated with anxiety, depression and cancer distress as dependent variables. The saturated models included linear and quadratic time effects as covariates in the regression models. If the dependent variables significantly changed in time, 'occurrence of complications', 'subsequent surgery', 'complete failure of BR' were added as predictors, including 'age' and 'time since mastectomy' as covariates to correct for their influences. All these variables were set as fixed effects, including the interaction effects with the linear and quadratic time points. Continuous variables were standardized to facilitate the interpretation of the estimates ('age' and 'time since mastectomy').

For sufficient power (alpha=0.05, beta=0.20) at least 135 participants were required with a maximum of 14 covariates [25]. The deviance statistic [26] using restricted maximum likelihood [27] was applied to determine whether a random slope was needed in addition to a random intercept. The saturated model was reduced by eliminating fixed effects with p-value > 0.05, taking into account that interaction effects ought to be nested under their respective main effects [28]. The significance of the difference between the saturated model and the parsimonious final model was determined with the deviance statistic using the maximum likelihood. Effect sizes in the MLA model were calculated by dividing the estimated differences by the estimated standard deviation at baseline [29].

Finally, overall patient satisfaction at T2 was described providing general descriptive statistics and Spearman's Rho correlation coefficients were calculated, with the complication variables ('occurrence of complications', 'subsequent surgery', and 'complete failure of BR') and type of BR, as patient satisfaction was non-normally distributed.

Two-sided *p*-values < 0.05 were considered statistically significant and data were analyzed with the statistical package SPSS 17.0 (SPSS Inc., Chicago).

Results

Patient samples

Seven women were excluded from the analyses due to the development of recurrent disease after completion of the first questionnaire (Figure 1). Thirty women were lost to follow-up: one patient with diabetes mellitus who died 18 days after DIEP flap BR due to pneumonia, eight women stopped participation, and 21 women did not complete all three questionnaires (T0, T1 and T2). Dropouts (*n*=30) did not differ significantly from other participants meeting the inclusion criteria (*n*=115) regarding demographic variables, additional surgery for complications, complete failure of BR, and baseline anxiety, depression and cancer distress (data not shown). However, more dropouts had (minor) complications (63% vs. 37%, *p*=0.013).

Patient characteristics and complications were reported for all participants fulfilling the inclusion criteria (*n*=145, Tables 1 and 2). Further analyses were performed on their data of all three assessments (T0: *n*=145; T1: *n*=139; T2: *n*=119, Tables 3 and 4).

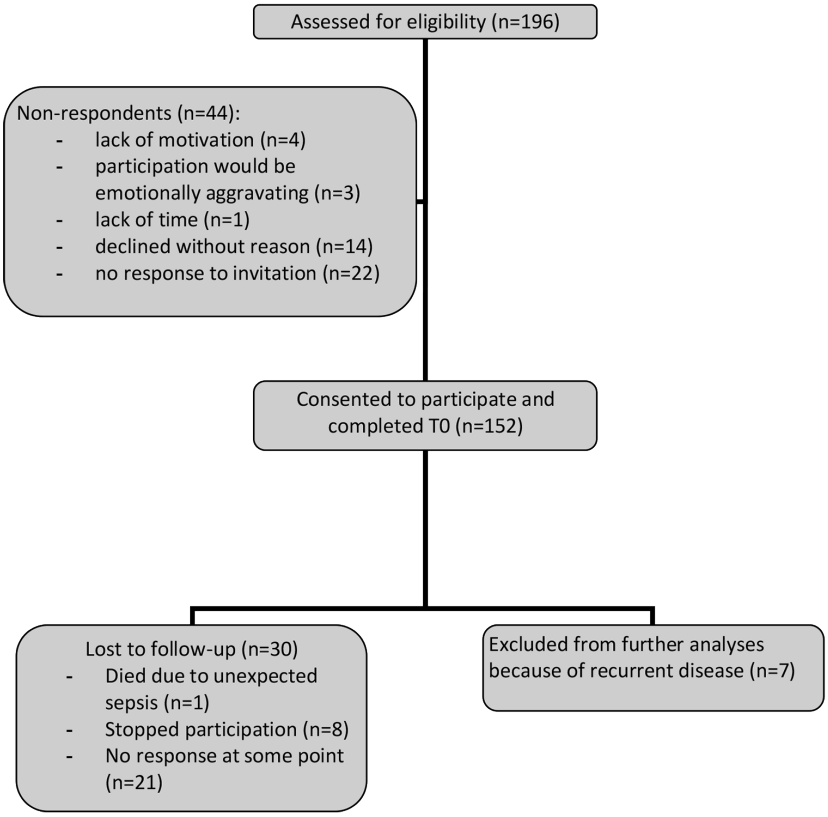
Demographic and clinical characteristics

Baseline patient characteristics are shown in Table 1. The time period between mastectomy for breast cancer and BR was on average 2.3 years, (range=0-20.3 yrs, median=1.6 yrs). Questionnaires at T2 were completed on average 21.2 months after BR (*sd*=5.9 months, median=20.4 months).

Postoperative complications and subsequent surgery

Complications after BR and consequent surgery, as obtained from the medical files are described in Table 2. During the entire BR process (mean=21.2 months), 62 (43%) patients experienced one or more complications (e.g. wound infection, skin necrosis, hematoma or wound dehiscence) and 50 (35%) patients of the total sample consequently needed additional surgery. Twenty-two (15%) women even underwent more than one surgical intervention due to complications (range 2-5; Table 2). Reasons for additional surgery were, for example, hematoma drainage, replacement of an infected tissue expander, or a microvascular revision. Ten women (6.9%) lost their reconstructed breast during the follow-up period, which were significantly more patients with an implant BR (*n*=9; *p*=0.007). There were no differences in the occurrence of complications or subsequent surgical interventions between women with either implant or DIEP flap BR (*p*=0.51 and *p*=0.22, respectively). Significantly more wound infections occurred after implant BR (*p*<0.001).

Figure 1. Flow chart of patient inclusion



Inconsistencies were found between the data from the medical reports and the self-reported patient questionnaires regarding the occurrence of complications, subsequent surgery and the complete failure of BR (p<0.001), showing an over-report of complications by patients. However, when comparing the correlations with anxiety, depression and cancer distress no significantly different correlations were found for the medical and patient-reported outcomes. Therefore, for all statistical analyses, data from the medical reports were used as these were complete for all patients.

Changes in anxiety, depression and cancer distress after breast reconstruction

For all three unadjusted PD measures, significant linear and quadratic time effects were found. Anxiety significantly declined with effect sizes of d=-0.19 from T0 to T1 and d=-0.44 from T0 to T2 (Table 4). Depression significantly increased from T0 to T1 (d=0.18), whereas from T0 to T2 depression did not significantly decrease (d=-0.17). Cancer distress significantly decreased from T0 to T1 (d=-0.43) and from T0 to T2 (d=-0.57).

Table 1. Baseline patient characteristics of 145 women undergoing breast reconstruction after therapeutic mastectomy

	N (%)
Mean age in years at time of BR (*sd*)	49.4 (8.7)
Having a partner	121 (83.4)
Having children	126 (86.9)
Education level	
Low	26 (17.9)
Intermediate	56 (38.6)
High	63 (43.4)
Inherited predisposition for BC [a]	39 (26.9)
Unilateral BR	108 (74.5)
Bilateral BR	37 (25.5)
Immediate BR	47 (32.4)
Delayed BR	98 (67.6)
Implant BR	70 (48.3)
DIEP-flap BR	75 (51.7)
Mean time since mastectomy in years (*sd*)	2.3 (3.3)
Mean BMI in kg/m^2 (*sd*)	21.2 (5.9)

[a]: brca1/brca2/familial risk; ; BC: breast cancer; BMI: body mass index; DIEP: Deep Inferior Epigastric artery Perforator; BR: breast reconstruction; sd: standard deviation

Predictors of anxiety, depression and cancer distress after breast reconstruction

The adjusted time effects for all three PD measures with the covariates are presented in Table 3.

Loss of the reconstructed breast(s)

Of the complication variables, only complete failure of BR was significantly related to depression and cancer distress. A significant time effect demonstrated an increase of depression at T1, with a large effect size, (*d*=0.67+0.18=0.85), but these symptoms declined at T2 (Table 4). Regarding cancer distress only a main effect was found demonstrating that complete failure of BR was associated with higher scores during the entire BR course (*d*=0.65).

Covariates

The MLA model demonstrated main effects for age with anxiety and depression, indicating that a younger age was related to more anxiety as well as more depression during the entire BR course. For cancer distress significant time interaction-effects were found with age and the mean estimates were significantly lower at T1 and T2 if age increased with 10 years

Table 2. Complications obtained from the medical files after implant and DIEP flap BR

	Implant BR N=70	DIEP flap BR N=75	*p* Value*
	n (%)	n (%)	
One or more complications	32 (45.7)	30 (40.0)	0.51
Subsequent surgery for complications	28 (40.0)	22 (29.3)	0.22
Subsequent surgery more than once	14 (20.0)	8 (10.7)	0.16
Complete failure of BR	9 (12.9)	1 (1.3)	0.007
Type of complications			
Wound healing complications			
Wound dehiscence	2 (2.9)	0	0.23
Wound infection	16 (22.9)	2 (2.7)	<0.001
Haemorrhage leading to surgery	3 (4.3)	2 (2.7)	0.67
Hematoma	2 (2.9)	7 (9.3)	0.17
Partial mastectomy skin flap necrosis	1 (1.4)	3 (4.0)	0.62
Seroma	0	2 (2.7)	0.50
Abscess	1 (1.4)	1 (1.3)	1.00
Implant-related complications			
Prosthesis malposition	2 (2.9)		
Implant or tissue expander perforation	2 (2.9)		
Capsular contracture	4 (5.7)		
Definite loss of implant/expander	9 (12.9)		
Flap-related complications			
Fat necrosis		7 (9.3)	
Venous congestion		1 (1.3)	
Partial flap necrosis		2 (2.7)	
Total flap loss		1 (1.3)	
Abdominal wound healing problems		4 (5.3)	
Abdominal herniation		1 (1.3)	
General complications			
Radiodermatitis	1 (1.4)	0	0.48
Pneumothorax	1 (1.4)	0	0.48
Symptomatic pulmonary embolism	0	1 (1.3)	1.00
Subcutaneous extravasation i.v. line	0	2 (2.7)	0.50

DIEP: Deep Inferior Epigastric artery Perforator; BR: breast reconstruction; * Fisher's exact test

Table 3. Predictors of the course of cancer distress in women undergoing BR analyzed with MLA

Fixed effects	Estimate [95% CI]		Std. Error	p-value
Anxiety				
Intercept	4.92	[4.33 – 5.51]	0.30	<0.001
Time linear	-0.703	[-1.322 – -0.084]	0.314	0.03
Time quadratic	0.0299	[0.0011 – -0.0588]	0.0147	0.04
Age	-0.116	[-0.173 – -0.058]	0.029	<0.001
Time since mastectomy	-0.0196	[-0.1795 – 0.1404]	0.0810	0.81
Time since mastectomy * linear time	0.0139	[0.0049 – 0.0229]	0.0046	0.003
Depression				
Intercept	5.16	[4.46 – 5.86]	0.35	<0.001
Time linear	0.80	[0.04 – 1.55]	0.38	0.04
Time quadratic	-0.0395	[-0.0747 – -0.0044]	0.0178	0.03
Complete failure of BR	0.751	[-1.900 – 3.402]	1.347	0.58
Complete failure of BR * time linear	2.87	[0.04 – 5.69]	1.43	0.047
Complete failure of BR * time quadratic	-0.136	[-0.268 – -0.004]	0.067	0.04
Age	-0.103	[-0.167 – -0.038]	0.033	0.002
Time since mastectomy	0.0639	[-0.1175 – 0.2454]	0.0920	0.49
Time since mastectomy * linear time	0.0173	[0.0067 – 0.0279]	0.0054	0.001
Cancer distress				
Intercept	22.20	[20.10 – 24.31]	1.07	<0.001
Time linear	-5.59	[-7.63 – -3.56]	1.04	<0.001
Time quadratic	0.250	[0.155 – 0.345]	0.048	<0.001
Complete failure of BR	8.07	[1.12 – 15.02]	3.52	0.02
Age	-0.171	[-0.410 – 0.069]	0.122	0.16
Age * linear time	-0.36	[-0.60 – -0.13]	0.12	0.003
Age * quadratic time	0.0166	[0.0055 – 0.0276]	0.0056	0.003
Time since mastectomy	-0.90	[-1.54 – -0.27]	0.32	0.005
Time since mastectomy * linear time	0.651	[0.031 – 1.271]	0.315	0.04
Time since mastectomy * quadratic time	-0.0300	[-0.0588 – -0.0011]	0.0147	0.04

BR: breast reconstruction; MLA: multi-level regression analysis

Table 4. Estimates of the outcome variables in time and covariate effects

	Anxiety			Depression			Cancer distress		
	Estimate	***d*** [3)]	***p***	**Estimate**	***d*** [3)]	***p***	**Estimate**	***d*** [3)]	***p***
No covariate effects [1)]									
Baseline	4.9			5.2			22.2		
1 month	4.3	-0.19	0.026	5.9	0.18	0.039	16.9	-0.43	<0.001
21 months	3.4	-0.44	<0.001	4.5	-0.17	0.067	15.1	-0.57	<0.001
Age, 10 years additional									
Baseline	3.8	-	-	4.1	-	-	20.5		
1 month	3.1			4.9			11.7	-0.28	0.003
21 months	2.2			3.4			10.3	-0.25	0.011
Time since mastectomy, 10 years additional [2)]									
Baseline	4.7			5.2			13.2		
1 month	4.2	0.04	0.003	6.2	0.04	0.001	14.0	0.50	0.039
21 months	6.1	0.81	0.003	8.2	0.89	0.001	10.8	0.38	0.172
Complete failure of BR									
Baseline	4.9	-	-	5.9			30.3	-	-
1 month	4.3			9.4	0.67	0.047	24.9		
21 months	3.4			5.4	0.06	0.876	23.2		

[1)] At mean of continuous covariates, and zero for binary covariates
[2)] 15 women have a delay > 5 years, of whom 4 > 10 years
[3)] Cohen's *d*, effect size compared to baseline, for covariates additional effect sizes.

older than the mean (Table 4). Finally, a longer time since mastectomy showed significant time effects for anxiety, depression and cancer distress. If a longer time since mastectomy was increased with 10 years, significantly more anxiety and depression at both T1 and T2 were found. Cancer distress was significantly higher at T1 for women who underwent mastectomy a longer time ago, but not at T2 (Table 4).

Patient satisfaction with aesthetic outcome

Mean patient satisfaction with aesthetic outcome at T2 (n=113) was 7.67 (*sd*=1.41, median=8.00, range=2-10). Of the complication variables, only additional surgery for complications was negatively correlated with patient satisfaction (*r*=-0.30, *p*=0.002) and it was positively correlated with the type of BR (*r*=0.32, *p*=0.001). This indicates that women who had surgery for complications and women with an implant BR were less satisfied with the aesthetic outcome at T2.

Discussion

This study prospectively investigated the relationship between complications, subsequent surgery and complete failure of BR with psychological distress (PD) after completion of the entire BR course. Overall, PD after BR significantly decreased in time. Complete failure of BR was significantly related to increased cancer distress during the entire BR course and to increased depression on the short term. The occurrence of complications did not result in high levels of PD on the long term.

The total complication rate after BR of 42% in the present study is comparable with other studies [7;30;31]. Although the occurrence of complications was not related to PD or patient satisfaction on the long term, additional surgery for complications predicted less patient satisfaction with aesthetic outcome on the long term. This is in line with another study concerning a similar patient group [32]. It is also in accordance with previous literature reporting women with a DIEP flap BR in general are more satisfied with the aesthetic result [23;33-36].

An explanation for the non-significant relationship between the occurrence of complications and consequent surgery with PD may be that other factors might have a more profound effect on PD, such as changes in body image [37-39] or pain symptoms [6] but this was not consistently measured within the current study design. Furthermore, to specifically measure the impact of complications on PD, ideally each patient should have completed the PD questionnaires immediately after a complication had occurred, which is suggested for future research. In the current study, it may have been the case that complications had already been salvaged at the time patients completed the final questionnaire, as the T2 questionnaire was planned after completion of the entire BR course. Finally, since many dropouts had complications it might be possible that the correlation between complications and PD would have been higher if dropouts had still participated. Nevertheless, our study sample had sufficient power and we assume it was representative regarding age and timing of BR compared to the non-respondents as described elsewhere [6].

In accordance with other studies, younger women had more psychological adjustment problems compared to older women [40;41]. Younger breast cancer patients are generally diagnosed with more aggressive tumors, and therefore likely to be treated more extensively. In addition, they are faced with more concerns regarding relationship establishment, fertility issues, and body image problems compared to older women [42-49]. It may be that they are less experienced with disruptive life events and that they have less adaptive coping skills than older women, although in time their distress levels may recover well [50]. It might be reassuring for younger patients to receive information that it is common for younger women to experience high distress levels, but that in time this may resolve [50].

A *longer* period between BR and the mastectomy (time since breast cancer diagnosis) was related to increased anxiety and depression at T2. The strongest effect was found if the time since mastectomy was 10 years longer ago compared to the average time. Although this concerned only a small number of women, effect sizes were large. Women with higher PD since mastectomy might decide at a later point in life to opt for BR. They might have experienced a longer period of fear of recurrence or physical symptoms since breast cancer treatment, next to the dissatisfaction with wearing a prosthesis which might have led to increased PD before BR [51-54]. Shortly after BR their cancer distress might have increased as they were possibly reminded of their previous mastectomy and the breast cancer itself. Cancer distress was not significantly increased at the longer-term for women who underwent mastectomy a longer time ago. This can be explained by their relatively low baseline level which could not be reduced much more.

Women who eventually had a completely failed BR reported more depression at short term follow-up, whereas it is likely that it was unclear at that point that the failed BR could not be salvaged by another method. Also, these women experienced increased cancer distress during the entire BR course, remarkably even before undergoing BR. Considering the relationship between psychological wellbeing and the physical immune system, a hypothesis may be that more preoperative distress is related to a decreased physical recovery from BR [55;56]. Nevertheless, it is suggested to reconsider offering BR to highly distressed patients, as preoperative distress may be a receipt for a worse recovery process, but future research should confirm this.

In conclusion, overall the majority of patients adjusted well after BR, regardless of complications. However, a complete failure of BR was related to higher PD. During postoperative outpatient visits, the psychological wellbeing should be explored, particularly in women with a failed BR [57]. In addition, postoperative telephone contacts with nurse-practitioners could be provided to patients at risk for high PD. Reconstructive surgeons and/or nurse practitioners should refer patients any time during the BR course for psychological help if significant psychological adjustment problems persist.

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