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The psychological
impact of
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reconstruction

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prophylactic
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breast cancer

Jessica P. Gopie

The Psychological Impact of Breast Reconstruction after Prophylactic or Therapeutic Mastectomy for Breast Cancer

Jessica Premdee Gopie

COLOFON

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The Psychological Impact of Breast Reconstruction after Prophylactic or Therapeutic Mastectomy for Breast Cancer

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Voor ons kleine wondertje

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CHAPTER 1 INTRODUCTION



1. Breast cancer

In the Netherlands breast cancer is the most common type of cancer in women with a lifetime risk of 1 out of 8. Every year there are more than 13,000 new cases mostly occurring in women older than 50 years of age [1]. Therefore, since 1989 women aged between 50 and 75 years old have been invited to participate biannually in a national breast cancer screening program using mammography which has proven to be effective in the early detection of breast cancer and the reduction of mortality [2-4]. Several treatment options are available for breast cancer, such as surgery, chemotherapy, radiotherapy and hormonal therapy. Despite the introduction of breast conserving therapy with or without neo-adjuvant treatment, mastectomy is still performed in about 46% of all cases [5], while more recent results have shown that long-term survival rates are similar after breast conserving therapy including radiotherapy [6].

About 5% to 10% of all breast cancer cases are caused by a genetic predisposition [7]. Women from families with a BRCA1/2 mutation have a significantly increased cumulative lifetime risk for developing breast cancer (39-85%) as well as ovarian cancer (10-63%) [8-11]. These women are offered a specific breast surveillance program including an annual MRI-scan, a mammography and clinical breast examination. Women at high risk for breast cancer based on their family history are also offered a specific breast surveillance program, as suggested by the Dutch Breast Cancer Guidelines 2012 [12;13]. As breast cancer screening programs may detect breast cancer at an early stage but cannot prevent it, prophylactic mastectomy may also be discussed with these high risk patients as an alternative option to reduce the risk for developing breast cancer [14-16].

1.1. Therapeutic mastectomy and breast reconstruction

Mastectomy can have a significant impact a woman's body image and self-identity, including feelings of abnormality, depressive symptoms, loss of wholeness, and mourning for the lost breast [17-21]. Breast reconstruction (BR) can significantly improve patient satisfaction and body image after mastectomy [22-27]. However, general psychological outcomes do not differ significantly between women with and without BR after mastectomy [28-32]. Recently, it has been found that BR is associated with decreased breast cancer mortality compared to women undergoing mastectomy only, but this is more likely to be explained by socioeconomic factors and access to health care than to oncologic factors [33;34].

The number of patients receiving BR after mastectomy ranges from 10% to 40% but is still increasing. However, there is a great ethnic and geographic variation, for instance non-white women and patients from deprived or rural areas are less likely to undergo BR [35]. In the Netherlands, the estimated uptake of BR after therapeutic mastectomy is about 20%, indicating the majority of patients does not receive BR [36].

This thesis focuses on the impact of two different types of BR after mastectomy: the most commonly performed BR method using silicone implants and the most advanced BR type using abdominal tissue; the Deep Inferior Epigastric artery Perforator (DIEP) flap (Figure 1). There was very little data on psychosocial outcomes regarding DIEP flap BR available at the beginning of this study [37-41]. Therefore, it was investigated what possible benefits

and disadvantages this BR method would bring patients, in comparison to implant BR. The effect of demographic and other clinical variables on the psychosocial outcomes after BR was also investigated.

The following paragraphs provide an overview of therapeutic and prophylactic mastectomy, the types and timing of BR, psychosocial aspects related to the decision to undergo BR and the psychosocial outcomes after BR. In the final paragraph, the aims and research questions of this thesis are described.

1.2. Prophylactic mastectomy and breast reconstruction

Prophylactic mastectomy (PM) is considered to be an effective method for decreasing the breast cancer risk of high risk women significantly with a risk reduction of more than 90% [14-16;42;43], but there is insufficient data to support an improvement in survival rates after PM [44-46]. The combination of the cancer risk, fear of cancer and increasing possibilities for BR has popularized this risk-reducing surgery. More than ten years ago 55% of the Dutch unaffected high risk patients chose bilateral PM [43], but more recently this percentage has decreased to 33% [47]. The reasons for a declining uptake of bilateral PM may be related to recent study results describing the risk for adverse effects on body image and sexuality [48-59]. In addition, more advanced diagnostic imaging techniques have become available, providing earlier detection of breast cancer development [60-65] and it is likely that this improved diagnosis may dissuade doctors and patients from choosing bilateral PM.

This said, the uptake of bilateral PM in the Netherlands is still high compared to the mean international uptake of 18% [47;66] and only the United States of America (36%) and the United Kingdom (40%) have a higher uptake rate. The uptake is lowest in Poland (3%), Israel (4%) and Norway (5%). Regarding contralateral PM in high risk women with a history of breast cancer, the uptake of 53% in the Netherlands is also high, compared to the average international uptake of 27% [46;67]. The large variance in uptake may reflect cultural differences in which both patients and clinicians may play a role.

Currently, BRCA1/2 mutation carriers are advised to undergo prophylactic bilateral salpingo-oophorectomy (PBSO) to reduce the risk for ovarian cancer as well as the prevalence of breast cancer and to improve the survival rate in premenopausal BRCA1/2 mutation carriers [44;68-71]. BRCA1 mutation carriers are recommended to undergo PBSO between 35 to 40 years of age, whereas for BRCA2 mutation carriers this is advised between the age of 40 and 45 years as recommended by the Netherlands Foundation for the Detection of Hereditary Tumours (STOET) [72]. However, PBSO may have a profound effect on psychological wellbeing as it induces the pre-menopause, which may result in adverse psychological, somatic and sexual consequences, including vasomotor symptoms, vaginal dryness and decreased libido [73-75].

1.3. Types of breast reconstruction

In general, three types of BR are available: with silicone implants, autologous tissue, or a combination of both. BR, using a silicone implant is the most commonly performed [76;77] and is usually preceded by the insertion of a tissue expander during the first stage of the

reconstruction, which is gradually inflated to expand the breast skin and muscle [78], and after a few months is replaced with the definite implant.

Several autologous BR techniques exist, commonly including skin, fat and muscle tissue from a distant donor site, such as the latissimus dorsi myocutaneous (LD) flap from the back [79]. The transverse rectus abdominis myocutaneous (TRAM) flap includes skin, fat and muscle from the lower abdomen which is transferred to the chest wall [80], and the TRAM flap is either a pedicled or a free flap requiring a smaller proportion of the abdominal muscle. Other autologous BR techniques include the gluteal artery perforator (GAP) flap and the transverse myocutaneous gracilis (TMG) flap, which consist of skin and fat from the buttock and skin, fat and muscle from the medial thigh area [81;82], respectively. Currently, the most popular autologous BR method is the Deep Inferior Epigastric artery Perforator (DIEP) flap, using abdominal skin and fat, but leaving the abdominal muscles intact, which reduces the chance of abdominal muscle weakness or hernia [83]. However, it requires microsurgical expertise and for the reconstructive surgeon to have specialist knowledge, and this expertise is only available in specialized centers, resulting in long patient waiting lists and higher costs. In general, higher satisfaction rates and a better body image have been reported after autologous BR compared to implant BR, but more prospective studies are required to be conclusive [40;41;49;84-87].

1.4. Timing of breast reconstruction

BR can be performed either immediately, at the same time with mastectomy or delayed; months or years after mastectomy. A randomized controlled trial (RCT) investigating the specific impact of immediate versus delayed reconstruction found that three months postoperatively immediate BR was associated with better psychosocial outcomes compared to delayed or no BR [24]. As randomization to the type or timing of BR is generally seen as unethical with regard to withholding information and not observing patient preferences, no other RCT has been performed in this field since 1983. Cross-sectional and cohort studies have demonstrated that aesthetic outcome is generally better following immediate BR as typically the skin envelope and occasionally the nipple can be preserved [84;88;89]. Women with immediate BR may have less distress and a better body image, more self-esteem and may feel more sexually attractive as well [90]. However, with regard to the type of BR, more positive outcomes on body image and sexual satisfaction were found after delayed autologous BR [40;49;84;87]. The timing of BR is of great significance here, as women with delayed BR have lived for a period with only one or no breasts and therefore have a greater opportunity to experience improvement, as their body image and sexual satisfaction may be at the lowest point before they undergo BR. Furthermore, after delayed BR the complication risk has been found to be lower compared to immediate BR [88].

Generally, the timing of BR does not have an impact on the incidence of recurrent breast cancer and women undergoing immediate BR generally experience no delay in adjuvant treatment compared to women without undergoing BR [33;91-93].

2. Psychological aspects of Breast Reconstruction

2.1. Decisional aspects of breast reconstruction

The decision for the type of BR can be influenced by different factors such as surgeon's preferences and expertise, treatment characteristics (therapeutic or prophylactic indication for mastectomy, timing of BR), and patient characteristics [51;77;94-99]. Some patients are limited in their reconstructive options by clinical and logistic circumstances, such as having insufficient autologous tissue or being restricted by long waiting lists [96]. However, some demographic conditions facilitate the access to BR: being younger, Caucasian, higher educated, wealthier and more often married or in a relationship [31;96;98-100].

Women generally choose BR because they feel too young to live without breasts, want to avoid wearing an external prosthesis, and wish to feel feminine and self-confident [96;98;99]. Common reasons not to choose BR are: feeling reconstruction is not essential for physical and emotional well-being, uncertainty about the procedure and not wanting anything unnatural in the body [96;98].

A lack of information and unrealistic expectations regarding the outcome of BR are also generally associated with regret or low satisfaction with the end result of BR [21;49;95;101-104]. Therefore, it is extremely important to inform patients as comprehensively as possible about the options regarding the types of BR and possible outcomes. Currently, there is no standardized information provided regarding BR options for patients, and, one study demonstrated that autologous BR was chosen by active information seekers and patients who referred themselves to a reconstructive surgeon [105]. This suggests that less independent decision-makers are less aware of the different reconstructive options and as a consequence, due to the increased risk of not selecting the optimal option may be less satisfied with their decision.

2.2. Complications after breast reconstruction

Implant BR can be performed either as a one-stage procedure (direct insertion of prosthesis) or a two-stage procedure (insertion of tissue expander followed by replacement with a definite implant). Presently, the two-stage procedure is generally performed. This procedure may take months as tissue expansion requires several months before the expander can be replaced with the implant. The overall short and long-term complication rates after implant BR vary from 18% to 51% [106-110]. Complications like infections, seroma and hematoma occur in 15% to 39% of the cases, of which 3% to 20% result in implant removal in the short-term [107;109].

Regarding autologous BR, free perforator flaps are preferred as there is less interference with muscle tissue and therefore donor site complications are minimized [76]. The most preferred free perforator flap for BR is the DIEP flap. The overall short and long-term complication rates after autologous BR vary between 32% and 43% [108;111]. Common immediate complications following DIEP flap BR are hematoma, seroma and partial flap necrosis occurring in about 2%, 5% and 15%, respectively, and in experienced hands total flap loss occurs in about 2% of DIEP flap reconstructions [112-114].

The chance for general failure of BR depends on the type of prosthesis used, the reconstruction method, and on risk factors for wound healing problems such as obesity, smoking, hypertension and pre- or postoperative radiotherapy [107;115-117]. Postoperative radiotherapy increases the risk of major complications, in particular after implant BR [106;116]. Postoperative complications can be an important indicator of dissatisfaction with reconstruction [118;119].

2.3. General quality of life

In general, the overall quality of life does not appear to differ between women with BR and women with mastectomy only [27;29;31;120-126]. One study found that women with BR even had a poorer wellbeing compared to women with mastectomy only, for which age might be a contributing factor, as the women with BR were significantly younger [30]. The general quality of life in these studies usually includes parameters such as distress or mood disturbances and overall wellbeing. It is more likely that other psychosocial aspects are affected, such as the altering body image and consequent effects on intimacy and the relationship, which is underlined by in depth-interview studies regarding the personal experiences of patients [54;56;97;101;127-130]. However, it remains relevant to correct for the overall quality of life when investigating these outcomes as they highly correlate with each other [131-134].

2.4. Body image

Conflicting results regarding body image after BR have been reported, with most studies having found no substantial differences between women who had received BR and women who had undergone mastectomy only [29;31;121;135-139]. Other studies reported better body image in women who had received BR [22;24;26;27;122;140;141]. For high risk women who are treated with PM and BR, body image is commonly negatively affected [48-50;57;58]. An explanation for this could be that losing the own healthy breasts without having had breast cancer, and directly exchanging them for reconstructed breasts might reduce satisfaction with appearance, self-esteem and self-consciousness.

The conflicting results regarding body image after BR could also be explained by methodological issues, as most studies had a retrospective design and could therefore not compare baseline scores with postoperative scores. It is also necessary to further investigate predictors of the patient evaluation of body image [142], therefore prospective studies are needed on the predictors of body image.

2.5. Sexual satisfaction and the partner relationship

Sexuality can be complex after breast cancer, as sexual changes can be caused by clinical factors, such as the influence of hormonal and chemotherapy with consequent menopause. A range of physical changes, including dyspareunia, fatigue, vaginal dryness, loss or decreased sexual desire or pleasure and numbness of the breasts, have been reported as a consequence of breast cancer treatment [121;143-150]. Of the BRCA1/2 mutation carriers 35% to 74% opts for PBSO to considerably lower the risk of ovarian cancer [47;151], but this

can, however, induce menopause and cause sexual side-effects, such as vaginal dryness, greater discomfort, and less satisfaction with sexual activities, although most complaints tend to decrease over time [152]. Psychosocial changes regarding sexuality include a fear of loss of fertility, negative body image, loss of femininity and attractiveness, depression and anxiety [143;153-155].

The quality of the partner relationship appears to be the strongest predictor of sexual satisfaction, sexual functioning and sexual desire compared to the physical or chemical changes due to cancer treatment [146;156;157]. If women can discuss their sexual practices with their partner, they are more able to manage changes in their sexual relationship [158]. After BR, sexual functioning has not generally been found to differ between breast cancer patients who had mastectomy only or with BR [22;24;29;31;121;122;125;137-140;159]. However, in high risk women who had PM, adverse sexual effects have been found in a substantial proportion of the patients [48-56].

The specific impact of BR on the partner relationship has received relatively little attention world-wide. A Franco-British study regarding patients' and partners' satisfaction with BR, showed satisfaction was related to the level of preoperative information, type of reconstruction and cosmetic result [160]. This suggests that it is important that further research should be conducted on the impact of BR on partner relationship satisfaction.

2.6. Patient regrets

About 18% of breast cancer survivors regret having had BR [161]. Regrets after BR are associated with a lack of information and unrealistic expectations regarding the outcome, as described previously [21;49;95;101-104]. In addition, women who are more concerned about the future or who had problems in communicating with their doctors are more likely to experience regret five years after cancer treatment [161]. Unaffected high risk women who underwent bilateral PM are less likely to report feelings of regret, which suggests that the relief from the reduced breast cancer risk outweighs the negative side effects of bilateral PM, such as pain, discomfort and adverse sexual effects [49;50;54;162].

3. Aims and outline of the present thesis

The Leiden – Rotterdam collaboration on breast cancer and the psychological issues of BRCA mutation carriers has started over 15 years ago [49;58;95;163-183]. Distress surrounding presymptomatic testing for BRCA1/2 was investigated, and high post-test anxiety was detected in 20% of the mutation carriers and in 35% of their partners [171]. Mutation carriers opting for PM had significantly higher distress levels than those opting for surveillance. In addition, adverse effects in body image and intimacy were observed in women who underwent PM combined with BR [49;163;169;175]. However, distress appeared to decline over time [58;164;169]. More recent studies of Den Heijer et al. showed that low self-esteem and feelings of stigmatization, increased distress and that communication regarding cancer within the family was associated with a reduced sense of vulnerability and less distress [167;168].

The current study aimed to expand this field of research and to explore patient motivation for BR and the specific psychological impact of this surgery on psychological distress, body image, sexuality and the partner relationship. This could increase the body of evidence to support a tailor-made psychosocial care-program for women dealing with either mastectomy after breast cancer or with prophylactic mastectomy.

3.1. Aims and research questions

In our study patients with implant and DIEP flap BR were included as our general aim was to prospectively investigate the psychosocial impact of BR after mastectomy comparing patients with implant and DIEP flap BR. At first, the decision-making process before surgery was explored, to investigate factors or thoughts related to unrealistic expectations. Secondly, our aim was to identify possible demographic, clinical and psychological risk factors that are related to a decreased psychosocial functioning.

The research questions were:

- What are the motives to opt for either implant or DIEP flap BR? (Chapter 2)
- To what extent do women make an independent decision regarding the type of BR? (Chapter 3)
- What is the short-term impact of complications after BR? (Chapter 4)
- What is the long-term impact of complications after BR? (Chapter 5)
- What is the impact of delayed BR on body image and the sexual and partner relationship satisfaction? (Chapter 6)
- What is the impact of prophylactic mastectomy with immediate BR on body image and the sexual and partner relationship satisfaction? (Chapter 7)

3.2. Study procedure

The study was a multi-center prospective follow-up study and the participants were women who opted for post mastectomy reconstruction after breast cancer (n=152) and healthy women who chose prophylactic mastectomy with BR because of an increased hereditary risk for developing breast cancer (n=50, Figure 2). Reconstructions were either implant or DIEP flap based, and were immediate or delayed. Exclusion criteria were:

- A BR in the past
- A detection of recurrence or metastasis of breast cancer during the study period, and
- Not being able to understand and speak the Dutch language sufficiently.

Patients were approached between December 2007 and May 2010 at the Leiden University Medical Center, Erasmus University Medical Center Rotterdam, Daniel den Hoed Cancer Center Rotterdam, Haga Teaching Hospital The Hague, Rijnland Hospital Leiderdorp, the Lange Land Hospital Zoetermeer, Hospital Walcheren, Admiraal de Ruyter Hospital Goes and at the Hospital Zorgsaam Terneuzen. Ethics approval was obtained from all participating hospitals..

Before their operation, 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. If patients did not respond within two weeks, a reminder was sent. Patients who returned their completed consent form received a self-report questionnaire that they had to complete before their operation. They were requested to complete the same questionnaire post-surgery, after 6 months and at the end of the BR procedure (21 months). In addition, questions regarding distress were sent at 1 month and 12 months post-surgery as well and patients were called by telephone to ask for the occurrence of complications and pain symptoms (Figure 3). After surgery, patient-reported clinical characteristics (including complications) were checked in the medical records.

The questionnaires included demographic information (e.g. age, having a partner or children, educational level), clinical data (e.g. indication for mastectomy, body mass index) and psychological assessments regarding general quality of life, anxiety, depression, cancer-specific distress, body image, sexual satisfaction and partner relationship satisfaction. At the final measurement patient satisfaction regarding the aesthetic result and complications experienced during the whole BR process were also requested. The content and psychometric properties of the self-report questionnaires are described in detail in the relevant chapters.

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Figure 1. Implant (A) and DIEP flap (B) breast reconstruction

Figure 2. Patient inflow

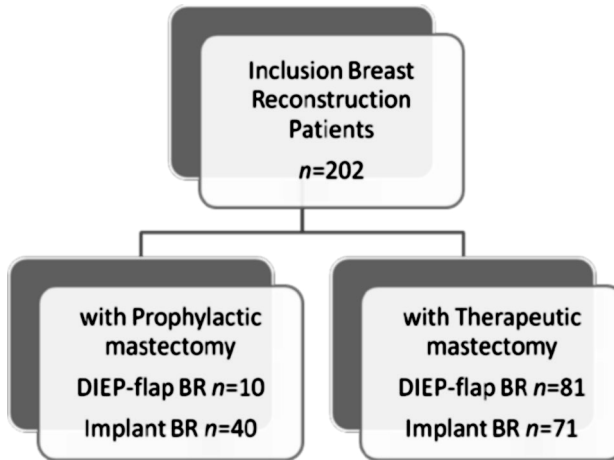
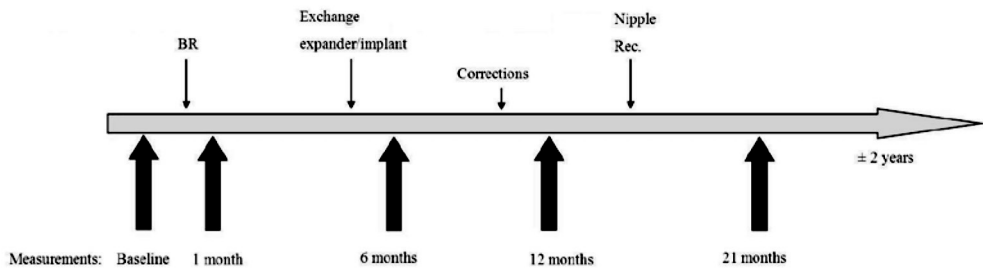


Figure 3. Timing of measurements



CHAPTER 2 WOMEN'S MOTIVES TO OPT FOR EITHER IMPLANT OR DIEP FLAP BREAST RECONSTRUCTION

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Abstract

Objective Understanding women's motives concerning breast reconstructive surgery will contribute to a better counseling and care for the increasing number of women choosing post mastectomy breast reconstruction (BR).

Methods We interviewed 31 women who opted for implant or DIEP flap BR after therapeutic or prophylactic mastectomy. Motives for BR in general and for the selected type of BR were investigated following a phenomenological qualitative research approach.

Results Women opting for implant BR were concerned with surgery related issues such as recovery time, number of scars and impact of surgery. They wanted to return to their daily life and restore their body image as soon as possible. Patients choosing DIEP flap BR were more focused on regaining a natural breast and wanted to benefit from the advantages of autologous tissue. Women scheduled for prophylactic mastectomy saw BR as an integral part of their treatment. Patients choosing for BR after therapeutic mastectomy wanted to regain a complete body image with BR.

Conclusions Patients' motives for implant BR were primarily related to surgical issues, whereas women who chose DIEP flap BR especially focused on regaining a breast that resembles their own lost breast as good as possible. Clinical variables (such as therapeutic or prophylactic mastectomy, breast irradiation, and waiting lists) need to be taken into account when considering a certain type of BR, as these can be of great importance in the decision making process.

Introduction

Body image is an integral component of the self-concept which for women includes a sense of femininity and attractiveness [1;2]. Mastectomy may have a negative effect on body image and may induce sexual problems and loss of womanhood [3]. Fortunately, breast reconstruction (BR) after mastectomy has shown to improve quality of life [4-8]. At present, an increasing number of women opt for BR, although the majority still rejects any form of BR, despite information about the possibility by their physician [9-12].

Several clinical factors contribute to decision making regarding BR, such as treatment (therapeutic or prophylactic mastectomy, history of breast irradiation, timing of BR) and physical characteristics (radiation of breast skin, amount of tissue loss), but also patient preferences play an increasingly important role [13-17].

Women who choose BR tend to be younger, are more likely to be well-educated, Caucasian, wealthy, and married or have a relationship [18]. Most reported reasons for choosing BR are to get rid of the external breast prosthesis, to be able to wear a greater variety of clothes, and to restore feelings of completeness and body integrity. Women who decided to have mastectomy only, considered BR as not essential for their physical and/or emotional wellbeing, were uncertain about the procedure, did not want to undergo more surgery or have any unnatural substance in their body [16;19;20].

BR with foreign material (e.g., silicone implant), autologous tissue (e.g., DIEP flap [21]), or with a combination of both (e.g., latissimus dorsi flap and implant) are presently available. Previous studies on patient satisfaction after BR have shown that in general satisfaction scores after autologous reconstruction were higher compared to following implant reconstruction [22-25].

Physician-patient communication is not always efficient and consequent in the decision making process regarding BR [12;26-28]. For example, discrepancies have been found between patients' preferences and physicians' perspectives,[29] which may result in low satisfaction rates or patients' regret after BR [26;30;31].

In this qualitative study we describe patients' motives to choose either implant or DIEP flap BR. It is important that physicians understand women's motives and integrate women's preferences before giving recommendations, to prevent regret and improve satisfaction after BR. Patients will then receive accurate and personalized information to establish more realistic expectations, which eventually may lead to improved satisfaction.

Methods

Participants

Women who participated in a multi-center prospective follow-up questionnaire study on the psychological effects of different types of BR and who also consented to be interviewed were included. They had previously undergone mastectomy or were about to have therapeutic mastectomy for breast cancer (BC) or prophylactic mastectomy (PM) for a high-risk for developing BC. Exclusion criteria were previous BR and poor command of the Dutch language.

We used the method of purposive sampling, the most commonly used form of nonprobabilistic sampling. Sample size relies on the concept of “saturation” or the point at which no new information or themes are observed in the data, which is usually reached within twelve interviews [32].

Patients were approached between December 2007 and January 2009 at six different Dutch hospitals.¹ Ethics approval was obtained from all participating hospitals.

Implant BR group

Twenty-three women who chose immediate or delayed implant BR (usually preceded by tissue expansion) after (prophylactic) mastectomy, were asked to take part in the interview study. Eighteen women consented to participate (78%) and fifteen were interviewed. Due to logistic problems three women were not interviewed.

DIEP flap BR group

Twenty-four women who were scheduled for an immediate or delayed DIEP flap BR after (prophylactic) mastectomy were asked to take part in the interview study. Eighteen women consented to participate (75%) and sixteen women were interviewed; the other interviews could not be scheduled due to logistic problems.

Procedure

A semi-structured interview was developed concerning motivational aspects of the decision making process, containing contextual factors (personal, social and clinical situation), personal views and expectations regarding BR. Examples of open-ended interview questions are: “Which options regarding reconstruction did you consider?”; “Did a specific inducement effect your choice for this type of breast reconstruction and could you describe this?”; “How do you think reconstruction will affect your social functioning?”. Examples of structured questions are: “Do you expect changes in your relationship due to the reconstruction?” and “Do you expect reconstruction to influence your self-esteem?”. The interview was pilot tested among five women planned for another type of BR or who had previously undergone BR. Refinements to improve clarity were made after feedback of interviewees and interviewers. In addition, patients were asked about their awareness of BR methods using implant or autologous material.

¹ The Leiden University Medical Center, Erasmus MC-University Medical Center in Rotterdam, Erasmus MC-Daniel den Hoed Cancer Center in Rotterdam, Haga Hospital in The Hague, Rijnland Hospital in Leiderdorp and the Lange Land Hospital in Zoetermeer.

An invitation to participate, informed consent, and prepaid envelope were sent before BR. Two weeks later non-respondents were sent a reminder. All consenting patients received the questionnaire (concerning the follow-up study, not incorporated in this study) with a prepaid envelope and were phoned to plan the interview.

All interviews were conducted by a psychologist (JG) and were planned either in a consulting-room at the hospital or at the patients' home, in case they were not able to visit the hospital due to practical reasons.

Table 1. Patient characteristics

	Implant BR N = 15	DIEP flap BR N = 16
Mean age at time of interview in years (sd)	44.2 (9.3)	48.5 (8.4)
Partner	14	13
Children	14	15
Children at home	12	8
Education:		
Low	3	2
Intermediate	7	7
High	5	7
Inherited predisposition for BC ^a	10	6
Mastectomy for BC:		
unilateral	4	12
bilateral	0	1
with contralateral PM	5	0
Bilateral PM	6	3
Timing of breast reconstruction:		
Immediate	12	3
Delayed	3	13
Mean BMI (sd)	25.7 (4.6)	27.0 (3.2)
Mean time since BC diagnosis in months (sd)*	35.6 (74.6)	46.6 (30.6)

BR: breast reconstruction; BC: breast cancer; ^a: brca1/brca2/familial risk; PM: prophylactic mastectomy; BMI: body mass index; DIEP: Deep Inferior Epigastric artery Perforator; n* = only patients with a history of breast cancer: 9 women with implant BR, 13 women with DIEP flap BR

Data preparation and analysis

All 31 interviews were recorded and transcribed verbatim. Interviews were analyzed using the phenomenological hermeneutical research approach [33]. By repeatedly listening to the interviews and iterative reading of the transcripts (JG, MH), personal and motivational

context concerning the decision-making process of BR were identified. Reported values, norms and expectations were categorized until no new key themes were detected. Saturation was reached after fourteen interviews in the implant group and after eight interviews in the DIEP flap group [32]. Afterwards, all interviews were reviewed to look for any additional significant statements, which were not found. Thematic analysis was performed by three authors who reached consensus (JG, MH, AT). This whole procedure was independently conducted for the interview analysis of both patient groups.

Results

The interviews were planned on average 16.8 days (range 2 to 65 days) preoperatively and mean interview duration was 54 minutes (range 28 to 111 minutes).

Breast reconstruction

Patient characteristics are shown in Table 1. The majority of patients were aware of BR options with implant and autologous material.

In general, similar key themes regarding personal and motivational context of BR were identified: most women reported they wanted to have BR because they found themselves too young to live without breasts. They wanted to avoid wearing an external prosthesis, or wanted to get rid of it. In particular, BR was expected to result in feeling more free and self-confident.

“You’re actually like a do-it-yourself kit: wearing contacts, my dentures, my breast – every morning...”

Femininity was also a very important motive to choose BR. Patients stated they would not feel feminine without their breasts. Above all, they felt the need to be ‘normal’. The majority of all participants believed that a woman needs to have breasts to feel normal or to have a normal body. Most participants also stated they needed to have their breasts reconstructed because they wanted to be or stay representative in clothing.

Timing of breast reconstruction

More than half of the women who were about to undergo delayed BR, reported they first wanted to recover from their BC treatment, physically as well as emotionally. Most women planned for immediate BR were not particularly concerned with timing of BR, although few said they preferred immediate BR to move on with their life as soon as possible. For women who were about to undergo PM, timing of BR was not an issue as BR was an integral part of PM.

Therapeutic or prophylactic mastectomy

Almost all patients who had undergone unilateral therapeutic mastectomy in the past were concerned with the asymmetry of their body. They were very aware of their daily

confrontation with mastectomy and felt asymmetry was unacceptable. They expected that BR would make them feel more complete.

Most women who were about to undergo bilateral PM regarded BR as an integral part of the entire treatment. Some of them associated BR itself with the risk reduction for BC and anxiety reduction. Some patients even stated that, if BR would not be possible, they would reconsider undergoing PM.

Women opting for implant breast reconstruction

Women who opted for implant BR (n=15) were on average 44 years old (28-61 years). Most women were moderately educated and had children at home. Their mean BMI was 25.7 (sd = 4.6). Nine women had a history of BC and six women were about to undergo PM with direct BR. Twelve women in this group were about to undergo immediate BR, while three women were planned for delayed BR (see Table 1).

Surgical considerations (n=9)

Women opting for implant BR predominantly had a pragmatic approach towards BR and predominantly focused on surgical aspects. They preferred to have a short recovery period and a smaller impact of surgery, since they wanted to regain their daily life as soon as possible.

“To undergo breast reconstruction with bodily material is more complex than implant reconstruction, the recovery period is longer and more intense, and given my social circumstances with three little children... Being out of daily routine for weeks already is inefficient, not to mention a recovery period of months!”

Some women preferred a short anesthesia period and, therefore, decided to have implant BR. In addition, some women were told that they had insufficient bodily tissue to undergo autologous BR, so implant BR was the most appropriate option.

Aesthetics (n=8)

Some women believed they would obtain the best aesthetic result by opting for implant BR. They were concerned about the number of scars on their body and definitely did not want to get donor site scars, which resulted in their preference for implant BR.

Women opting for DIEP flap breast reconstruction

Women who choose DIEP flap BR (n=16) were on average 48 years old (32-59 years) and most were moderately to well educated. Their mean BMI was 27.0 (sd = 3.2). Half of the group had children at home. Thirteen women had a history of BC and were planned for delayed reconstruction. Three women were planned for prophylactic surgery followed by immediate reconstruction (see Table 1).

Surgical considerations (n=14)

Participants felt the complication risk after DIEP flap BR was the lowest compared to other BR types. They often rated the complication risk of implant BR to be much higher than DIEP flap BR. Moreover, they felt DIEP flap surgery would offer long-term benefits compared to the use of implants, because the latter would require future revision operations for capsular contracture or implant malpositioning. Some women felt DIEP flap BR would offer an additional advantage: they would benefit from an abdominoplasty during the same operation. Finally, a few women stated implant BR was contraindicated due to previous radiation therapy.

“I’m a bit frightened when I think about implants. Imagine you’ll have bad luck... You sometimes hear about leaking silicones or capsular contracture. Then, after a year, the breast has to be opened again, or maybe already after some months. So I think, well... a DIEP flap feels safer to me.”

Aesthetics (n=14)

The majority expected a DIEP flap BR to give the best result. In particular, they preferred a new breast reconstructed with their own tissue that would feel soft and look natural. In addition, patients anticipated that such a reconstructed breast would sag just like their own contralateral breast, in contrast to a breast reconstructed with an implant. One woman illustrated this as follows:

“With silicones, at the age of 80 - if I get to make it (...) - then I’d probably end up with one pretty breast, while the other would be hanging down like a teabag. That would be no good!”

Sexuality (n=4)

Some women who had BC hoped DIEP flap BR would improve the sexual relationship with their partner. Since mastectomy they had experienced serious problems in their intimate relationship and felt BR would help and make them feel more confident in their sexual contacts. In addition, some of them indicated that their partners had problems with mastectomy and, consequently, their sexual activity had reduced significantly.

“Our sexual activity declined... It’s just... it’s just not happening! If we have had sex three times in one year, it’s a lot!”

Discussion

The main goal of the current study was to explore motives for choosing specific types of BR after therapeutic as well as PM. Motives for choosing BR in general were consistent with previous findings [16;19;20]. The most mentioned reasons to choose BR were feeling too young to live without breasts, wanting to avoid an external prosthesis, and wishing to feel feminine and self-confident. Regarding the decision making process of the specific type of BR, it remains difficult to distinguish between clinical and motivational aspects and to

discriminate their influence. Although this suggests heterogeneity of our patient groups, we feel this is representative for the Dutch patient population, as we recruited patients from different hospitals in the Netherlands.

Women who opted for DIEP flap BR focused on *aesthetic outcome*, such as gaining a natural breast that would resemble their own breast most. Women in the implant group reported more *surgery related* considerations, such as a shorter recovery period. However, total recovery time for two-stage implant procedures might actually be longer than after one-stage autologous BR, without patients realizing this.

Contrary to patients from the DIEP flap group, no women from the implant group expressed the specific desire to improve sexuality or their relationship. This can be explained by the fact that the majority of them were planned for immediate BR, and had not experienced the consequences of mastectomy on their sexual functioning.

The majority of the delayed BR patients opted for a DIEP flap reconstruction. They possibly chose a more sophisticated BR type with a better chance for a more natural result, because they had lived some time with an asymmetrical thorax. They had experienced the daily confrontation with mastectomy and its effect on their sexual relationships as well as on clothing limitations. Also, they had had more time to obtain information and consider all their reconstructive options. Another motive could have been the beneficial abdominoplasty effect of a DIEP flap procedure after closure of the donor site, as on average these women were older and slightly heavier than women from the implant group. However, as additional donor site scarring was seen as a disadvantage for some women opting for implant BR, abdominoplasty might as well be a contra-motive in the decision for the type of BR.

Decision making and information needs vary distinctly between women with BC diagnosis and those opting for PM. Women who are about to undergo therapeutic mastectomy followed by immediate BR often are in an “emotional roller coaster” at the time of decision making. They primarily need to undergo cancer treatment, and additionally have to consider BR, which may be secondary. Therefore, these women may be more concerned with surgery related considerations such as quick recovery and returning to daily routine.

Patients with prophylactic mastectomy generally choose for BR, in contrast to a considerably lower number of breast cancer patients [9-12;34]. Feelings of isolation may emerge as women can experience counterproductive reactions after telling others they opted for PM [35]. Most PM patients saw BR as an inclusive part of the prophylactic treatment which is most likely related to the information they preoperatively receive. All our patients are offered BR as an integral part of PM. Our PM patients predominantly chose implant BR, which is generally the reconstruction type performed after immediate bilateral PM [36]. Furthermore, women opting for prophylaxis are younger and often have young children at home. Therefore, it is sensible that they focus on practical aspects of surgery, such as short recovery time.

In hospitals where certain techniques are unavailable, patient information is likely to focus on available methods, like implant BR which is an attainable, relatively simple, and cheap method. DIEP flap BR was performed in only two of the participating hospitals at the time of patient inclusion, therefore not all patients may have had the information and

the possibility to undergo DIEP flap BR. In particular, immediate DIEP flap BR is complicated due to logistic factors, such as long waiting lists. However, ideally pre-operative patient information should be similar for all patients, regardless of mastectomy indication or timing of BR.

Other clinical factors may contribute to the decision making for BR type, such as previous radiation therapy precluding implants as this leads to more capsular contraction, or (un)availability of donor tissue for autologous BR.

From a psychological perspective, cognitive dissonance may have played a role in patients' attitude towards their selected BR type [37]. Patients could have tended to justify their decision as surgery was already planned and there was nearly a point of no return. However, due to the interviews explorative character it is improbable this was of significance.

Finally, future quantitative studies including larger patient groups, matched for clinical characteristics are recommended to validate this qualitative study. Questionnaires could be developed based on the topics discussed, including the role of clinical characteristics in the decision-making process, which should not be underestimated.

In conclusion, some BR patients are more concerned with surgery related aspects, while others have specific desires concerning aesthetic outcome. Mastectomy indication and timing of BR seem to be predominant factors in deciding for a specific type of BR. Delaying BR gives women more time to consider their reconstructive options. However, the optimal timing of BR also depends on clinical factors, such as complication risk [38].

Clinical implications include the need for plastic surgeons to explicitly ask patients who opt for immediate reconstruction whether they want their breasts reconstructed with implants or autologous tissue and inform them about all possibilities. If patients prefer autologous techniques, reconstruction might be delayed due to waiting lists. Also, if patients doubt their choice for BR or its timing, reconstructive surgeons might advise delayed BR or further clarify possible unrealistic expectations. In addition, since certain patients may need more information concerning psychosocial aspects of BR, breast-care nurses should be structurally involved in the decision making process as they can play an important role in information provision [39]. To gain ultimate satisfaction with BR, it is important to provide clear pre-operative information and to consider patient preferences and needs seriously [13;26;30;31].

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ADDENDUM CHAPTER 2

The decision not to undergo breast reconstruction

For reasons of comparison we invited 18 women who had undergone mastectomy without receiving breast reconstruction, to take part in the interview study to form the ‘mastectomy only group’. Sixteen were treated for breast cancer in the LUMC in 2005 and 2006, and one woman had mastectomy at the EMCR. Fifteen women (83%) consented to participate. Fourteen interviews were used for the study as one interview was excluded from analyses as the quality of the audio-tape was insufficient for transcription.

Women in the mastectomy only group were on average older than women in the reconstruction groups. All had unilateral mastectomy and none of them underwent prophylactic surgery (Table 1).

Table 2 shows the motivations against breast reconstruction reported by the women in the mastectomy only group. Seven women said they felt too old to choose for reconstruction. One woman clearly stated: *“No, that would be foolish. (...). I cannot afford that, can I? At my age, I don’t want to exhaust myself with things that are not really necessary, do I?!”*

Most women in this group accepted the loss of the breast and experienced no significant impairment of the mastectomy and therefore refrained from having reconstruction. Six women felt that their health and/or the emotional recovery from the breast cancer treatment were more important than the aesthetical loss. Four women stated they had other priorities than undergoing reconstruction, such as another chronic disease that required attention or the feeling that the expected end result would not outweigh the investment in reconstruction. Three women felt that they were not able to undergo reconstruction, because they had to take care of young children, a partner or a pet.

Several surgical specific aspects of reconstruction appeared to be important reasons not to opt for breast reconstruction. Ten women stated they did not want any more surgery. Eight women perceived the complication risk of reconstruction as too high. Other specific considerations were ‘don’t want the burden of the recovery’, ‘not being impressed by cosmetic end result’ and ‘don’t want any (more) scars’.

One woman emphasized her opinion regarding the end result of reconstruction: *“I’ve never seen an impressive breast reconstruction. I find it hideous. I don’t know what it is, but they are frayed, lumpy and not evenly formed. It is not something that belongs to a woman’s body, to my opinion.”*

The professional’s advice was decisive for four women and two women stated they did not choose for reconstruction because their partner did not support this.

Three women explained they were not physically or mentally ready (yet) for reconstruction. They wanted to recover from their BC treatment first or stated they were just not ready yet to decide about reconstruction.

Discussion

The three patient groups differed significantly in 'age', 'mastectomy as treatment for BC or as prophylactic surgery' and 'laterality'. These demographic and medical variables can (partly) explain the choices that have been made.

Age appeared to be an important factor in the decision for reconstruction, which is consistent with earlier findings [1-3]. Some women found themselves too old to undergo reconstruction, whereas others found themselves too young to go through life without breasts. Undergoing prophylactic surgery is often related to age, as women with a high-risk for developing breast cancer, need to decide at a young age whether they want to undergo prophylactic surgery to protect themselves against the development of breast cancer. In addition, breast reconstruction is generally offered as an integral part of prophylactic mastectomy. The demographic and clinical differences might therefore also be related to the surgical options available at the hospitals (i.e., surgeon's expertise, operation time available, waiting lists) which determines or might limit reconstructive options.

Women who decided against reconstruction refer to a variety of considerations, for example: no more operations, accepted loss of breasts and loyalty to a partner. These women seem to take a broader perspective, in which they also refer to other values, relevant for the quality of their lives. In contrast, those who opt for reconstruction underline more specific considerations, directly related to their expectations of the reconstruction in cosmetic, psychological and practical respect, which is consistent with previous studies [2;3].

The large variation in medical demographic characteristics between the three patient groups, hinders an explicit comparison of the motivational aspects, although it is known that women who decide against reconstruction are older than women who opt in favor of it [4].

Another factor restricting a direct comparison was that women in the reconstruction groups were interviewed preoperatively, while women in the mastectomy only group were interviewed after the operation. Future designs should try to match their patient groups on these variables.

It is important to note that not all women have reflected on all reconstruction options (the whole range). Some options may not have been available to them for medical reasons, may not have been offered to them by their centre or were not discussed with their doctor, whereas other women were only motivated to realize their preferred option, while neglecting other possibilities.

In conclusion, some patients focus more on practical, cosmetic aspects of the surgery, while others focus more on the psychosocial consequences of the reconstruction (type). This is an essential implication for the clinical practice: some patients might need more information concerning the psychosocial consequences of the breast reconstruction, in addition to the information provision about surgical aspects. Patients should be well informed about their reconstruction possibilities and about its consequences so they can make a well-informed decision.

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Table 1. Participants characteristics

	Breast Reconstruction			No Breast Reconstruction		
	Implant group	DIEP flap group	p Value*	Mastectomy only group	p Value*	p Value*
	n = 15 (%)	n = 16 (%)		n = 14 (%)		
Age at time of interview (yr)	Mean (sd)	48.53 (8.42)	.189**	57.93 (9.44)	.001**	
Partner	yes	14 (93.3)	.600	12 (85.7)	1.000	
Children	yes	14 (93.3)	1.000	12 (85.7)	.578	
Children at home	yes	12 (80.0)	.135	6 (42.9)	.206	
Education	low	3 (20.0)		4 (28.6)		
	intermediate	7 (46.7)		4 (28.6)		
	high	5 (33.3)	.492 β	6 (42.9)	.812 β	
Mastectomy for treatment for BC	yes	4 (26.7)	.004	14 (100.0)	.002	
Mastectomy both as treatment for BC and as prophylactic surgery	yes	5 (33.3)	.018	0 (0.0)	.305	
Mastectomy as prophylactic surgery	yes	6 (40.0)	.252	0 (0.0)	.040	
Timing of breast reconstruction	immediate	12 (80.0)		-		
	delayed	3 (20.0)	.001	-		
Laterality	unilateral	4 (26.7)		14 (100.0)		
	bilateral	11 (73.3)	.012	0 (0.0)	.001	
Weight	Mean (sd)	73.27 (15.85)	.340**	69.00 (8.07)	.116 β	
BMI	Mean (sd)	25.71 (4.59)	.386**	24.60 (3.52)	.158**	
Time elapsed since diagnosis (months)***	Mean (sd)	35.57 (74.64)	.018 β	35.57 (14.80)	.721 β	

Table 1. Participants characteristics (continued)

	Breast Reconstruction		No Breast Reconstruction	
	Implant group n = 15 (%)	DIEP flap group n = 16 (%)	Mastectomy only group n = 14 (%)	p Value*
Chemotherapy***	4 (40.0)	10 (76.9)	9 (64.3)	1.000
Radio therapy***	4 (40.0)	6 (46.2)	4 (28.6)	.491
Hormonal therapy***	2 (20.0)	9 (69.2)	7 (50.0)	1.000

BC: breast cancer; BMI: body mass index; DIEP: Deep Inferior Epigastric artery Perforator

* Fisher's exact test unless otherwise indicated; ** student t-test; β Mann-Whitney test, sig at .05.

*** N = only patients with a history of breast cancer: Implant group: 9; DIEP flap group: 13; Mastectomy only group: 14.

Table 2. Women’s motivations to opt for mastectomy without breast reconstruction

	n = 14 (%)
Being too old	7 (50.0)
Situation or loss of breast is accepted	8 (57.1)
Aesthetics are subordinate to health and inner growth	6 (42.9)
Having other priorities than BR	4 (28.6)
Feeling limited by personal/social situation	3 (21.4)
Don’t want more operations	10 (71.4)
Complication risk is too high	8 (57.1)
Don’t want burden of recovery (period)	4 (28.6)
Not being impressed by BR	4 (28.6)
Don’t want any (more) scars	2 (14.3)
No support professional	4 (28.6)
No encouragement partner	2 (14.3)
Not being physically or mentally ready (yet) for BR	3 (21.4)

BR: breast reconstruction

CHAPTER 3 INFORMATION SEEKING BEHAVIOR AND COPING STYLE OF WOMEN CHOOSING FOR EITHER IMPLANT OR DIEP FLAP BREAST RECONSTRUCTION

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Abstract

Background High satisfaction rates have been reported after autologous breast reconstruction. Yet, most mastectomy patients receive implant reconstructions (ImBR). Independent and active decision-makers have shown mainly to choose for autologous reconstructions such as the DIEP flap (DiepBR). To further explore the decision-making to opt for either ImBR or DiepBR, we investigated patient knowledge, informational resources used, effect of plastic surgeons' advice, coping style and personal independence.

Methods A total of 153 women who were planned for DiepBR or ImBR preoperatively completed a study-specific and standardized validated psychological questionnaire. Analyses were aimed at information seeking behavior, personal independence and coping styles associated with autonomous decision-making regarding reconstruction.

Results DiepBR women reported different informational resources to be very important and they were more active information seekers, compared to ImBR women. ImBR women found their physician's advice to be more important in their decision-making than DiepBR women. Actively seeking for information regarding BR was positively correlated with active coping, sensitivity to others and the decision for DiepBR.

Conclusions Women opting for DiepBR were more active and independent in their decision-making regarding the type of BR. Women opting for ImBR seemed less well-informed and more dependent on their physician in their decision compared to women opting for DiepBR. To undergo a complex type of BR, active and independent information seeking may be required. However, clinical and logistic characteristics need to be considered as some patients were limited in their reconstruction options.

Introduction

The number of patients opting for breast reconstruction (BR) increases [1-3]. In general, three types of BR are possible: BR using implants, autologous tissue, or a combination of both. In particular, an increasing number of patients choose microsurgical BR methods with autologous tissue, such as the Deep Inferior Epigastric artery Perforator (DIEP) flap in which the lower abdomen is used to reconstruct a breast [4;5]. These patients report higher satisfaction rates compared to women with implant BR [6-9]. However, the majority of patients opting for BR still receives implant BR [10-14].

Previous studies have shown that women who chose BR compared to those not opting for BR tended to be younger, better educated, more often Caucasian, wealthier and more often married or in a relationship [15-18]. The decision for the type of BR can be influenced by different factors such as surgeon's preferences and expertise, treatment characteristics (therapeutic or prophylactic indication for mastectomy, timing of BR) and patient characteristics [16;19-24]. Up to now only a few studies have specifically focused on the decision-making regarding the *type* of BR and personal processes involved [4;22;25]. Recently, a study showed that women who underwent microsurgical BR were likely to be older, independent and active decision-makers compared to women who underwent non-microsurgical BR [25].

Previous studies regarding BR have shown that a lack of information and unrealistic expectations regarding the outcome were associated with regret or low satisfaction rates with the end result of BR [9;20;26-28]. However, these studies were conducted after BR. Hence, the level of satisfaction with the result may have biased the recall of information provision. Others investigated coping style post-operatively and its relationship to regret post-surgery. They found that a passive coping style was correlated with post-decisional regret following BR [28]. Currently, no studies have explored the relationship between coping styles and the decision for the type of BR pre-operatively. An active coping style and personal independency regarding BR decision-making can result in women who actively seek for information. Consequently, they have the opportunity to form realistic expectations regarding the outcome, which ultimately may increase patient satisfaction and reduce regret.

In the present study information seeking behavior was explored pre-operatively in relation to coping styles and independent decision-making in women opting for either implant or DIEP flap breast reconstruction.

Patients and Methods

Patients

This study is part of a multi-centred prospective follow-up study on the psychological impact of two types of BR. Participants were women who opted for reconstruction after unilateral therapeutic mastectomy or after unilateral therapeutic mastectomy combined with contralateral prophylactic mastectomy (CPM). Reconstructions were either implant or DIEP flap based. All patients consented to participate in the study.

Exclusion criteria were a BR in the past and not being able to understand and speak the Dutch language sufficiently. Women who did not consent or who did not react two weeks after the invitation were considered as non-respondents. Patients were approached between December 2007 and May 2010 at the Leiden University Medical Center (LUMC), Erasmus Medical Center Rotterdam (EMCR), Daniel den Hoed Cancer Center, Haga Teaching Hospital (Haga), Rijnland Hospital Leiderdorp, the Lange Land Hospital, Hospital Walcheren, Oosterschelde Hospital and at the Hospital Zorgsaam. Ethics approval was obtained from all participating hospitals.

Implant BR

All 96 patients who were planned for implant BR (usually preceded by tissue expansion) were invited to participate in the study. Fifteen women did not respond, 10 patients declined and 71 women consented to participate (74.0%).

DIEP flap BR

All 101 women who were scheduled for a DIEP flap BR were asked to take part in the study. Seven women did not respond, 12 patients declined and 82 women consented to participate (81.2%).

Procedure

In the preoperative phase, 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. A reminder letter was sent if patients did not respond within two weeks. They were contacted by phone if surgery was planned on short term. Patients, who returned informed consent, received a questionnaire including a range of demographic, clinical and psychosocial items which they were requested to fill in preoperatively. Patient reported clinical data were confirmed by medical records.

Questionnaires

Demographic information (e.g. age, having a partner or children (at home), educational level), and clinical data (e.g. indication for mastectomy, body mass index (BMI)) were collected. The latter were confirmed by checking medical records.

Information provision

Preoperative information seeking behavior concerning BR was measured with a study specific-questionnaire. Fourteen questions were developed to investigate the following aspects (Table 3): a) knowledge regarding BR options (items 1,2); b) different informational resources (items 3-8); c) general quality of information (items 9,10); d) activity level of information seeking (item 12) and e) independency of decision-making (items 11,13,14).

Questions 1 and 2 could be answered with “yes” or “no”. Items 3 to 8 were rated on a five-point Likert scale ranging from 1 “not at all” to 5 “very much”, where a higher score

indicates a greater use of the concerning resource. Questions 9 to 14 were rated on a five-point Likert scale ranging from 1 “totally disagree” to 5 “totally agree”.

Autonomy

The Autonomy Connectedness Scale – 30 (ACS-30) [29] was used to assess different aspects of personal independence or autonomy and is a shortened version of the original questionnaire containing 50 items [30]. The ACS-30 consists of three subscales: Self-Awareness (SA, 7 items); Sensitivity to Others (SO, 17 items) and Capacity for Managing New Situations (CMNS, 6 items). Items can be scored on a 5-point scale from 1 “disagree” to 5 “agree”. Reported reliability and validity of the ACS-30 are good [29]. The concept of autonomy is used in this study to indicate the extent to which women are capable of making an independent decision concerning BR.

Coping

The Utrecht Coping List (UCL) [31] was used to assess seven coping strategies: Active Coping (AC, 7 items); Palliative Reaction Pattern (PL, 8 items); Avoidance and Awaiting (AA, 8 items); Seeking Social Support (SS, 6 items); Passive Reaction Pattern (PS, 7 items); Expressing Emotions (EE, 3 items) and Comforting Thoughts (CT, 5 items). Answers could be rated on a 4-point scale from 1 “seldom or never” to 4 “very often”. A higher score reflects more use of the concerning coping strategy. The validity and reliability of the UCL have been found to be good [32-34].

Statistical analyses

Differences between implant and DIEP flap BR for dichotomous variables were analyzed with Fisher’s exact tests. Normally distributed continuous variables were analyzed using Student’s t test, not normally distributed and ordinal variables with Mann-Whitney tests. Categorical variables were tested with Chi square tests. Missing values were replaced by the mean score of the concerning series. To explore determinants of active information seeking, backwards hierarchical regression analysis was used. ACS and UCL subscales were compared to the normal Dutch population with Student’s t-tests. Data were analysed with the statistical package SPSS 16.0 (SPSS Inc., Chicago). Two-sided p-values < .05 were considered statistically significant.

Results

Non-respondents

Ninety-three percent of the non-respondents (n = 44) underwent unilateral therapeutic mastectomy compared to 80% of the respondents (n = 153), of which 20% underwent therapeutic mastectomy combined with CPM (p = 0.04). Non-respondents and respondents did not significantly differ in age and timing of BR (p = 0.50 and p = 0.35, respectively). We assume the respondents are a representative sample of the total patient group.

Demographic and clinical characteristics

More women who chose implant BR were planned for reconstruction after therapeutic mastectomy combined with CPM. Women opting for DIEP flap BR had a higher BMI and their mean time interval between mastectomy and reconstruction was longer compared to women choosing implant BR. The patient groups did not differ in age, having a partner and/or children (at home), educational level and hereditary risk for developing BC (Table 1).

Table 1. Participants characteristics

	Implant group	DIEP flap group	<i>p</i> Value*
	n = 71 (%)	n = 82 (%)	
Mean age at time of breast reconstruction (sd)	49.07 (9.95)	49.40 (7.96)	0.82**
Partner	62 (87.3)	65 (79.3)	0.20
Children	62 (87.3)	70 (85.4)	0.82
Children at home	42 (59.2)	43 (52.4)	0.42
Education			
low	15 (21.1)	16 (19.5)	
intermediate	27 (38.0)	28 (34.1)	0.54¶
high	29 (40.8)	38 (46.3)	
Inherited predisposition for BC ^a	21 (29.6)	17 (20.7)	0.26
Unilateral therapeutic mastectomy	45 (63.4)	77 (93.9)	< 0.001
Therapeutic mastectomy with CPM	26 (36.6)	5 (6.1)	< 0.001
Mean BMI (sd)	24.0 (4.07)	27.7 (3.64)	< 0.001**
Mean time since mastectomy in years (sd)	1.43 (3.55)	3.15 (2.58)	< 0.001¶

^a: BRCA1/BRCA2/familial risk; BC: breast cancer; CPM: contralateral prophylactic mastectomy; BMI: body mass index; DIEP: Deep Inferior Epigastric artery Perforator; sd: standard deviation; * Fisher's exact test unless otherwise indicated; ** Student's t-test; ¶ Mann-Whitney test.

Informational resources and information provision

Initially, 38% of the women in the implant group were not aware of the possibility of breast reconstruction using autologous tissue compared to 17% of the women opting for DIEP flap BR ($p = 0.006$, Table 2).

For both groups the physician/plastic surgeon was the most important resource; however, women opting for implant BR rated their doctor as more important in their decision-making than women choosing for DIEP flap BR (Table 2, items 3 and 14, $p < 0.004$). Items 6 to 8 in Table 2 show that women who opted for DIEP flap BR rated a book, paper, magazine, internet and television as more important resources compared to women choosing implant BR ($p < 0.015$).

Table 2. Knowledge and information seeking behavior in the decision-making process of implant and DIEP flap BR patients

	Implant group	DIEP-flap group	p Value*
	n = 71	n = 82	
	n (%)	n (%)	
<i>Knowledge</i>			
1. "Before my decision I knew about the existence of BR with autologous tissue"	44 (62.0)	67 (82.7)	0.006**
2. "Before my decision I knew about the existence of implant BR"	67 (94.4)	78 (98.7)	0.19**
<i>Use of information resources (range 1-5: not at all – very much)</i>			
	M (sd)	M (sd)	
3. physician/plastic surgeon	4.2 (.9)	3.5 (1.2)	< 0.001
4. significant other/family/friend/colleague	2.5 (1.3)	2.2 (1.3)	0.12
5. information leaflet	2.4 (1.3)	2.2 (1.2)	0.36
6. book/paper/magazine	1.4 (.7)	1.9 (1.1)	0.005
7. internet	2.4 (1.5)	2.9 (1.4)	0.015
8. television	1.4 (.7)	1.8 (1.1)	0.015
<i>Information and decision-making (range 1-5: totally disagree – totally agree)</i>			
9. "Information concerning my type of BR was well available"	4.3 (1.1)	4.0 (.8)	0.001
10. "Information concerning my type of BR was understandable"	4.3 (.5)	4.1 (.5)	0.02
11. "I totally support my decision for this type of BR"	4.6 (.6)	4.6 (.6)	1.00
12. "I actively sought information about this type of BR"	3.7 (1.2)	4.2 (1.0)	0.003
13. "I have the feeling the choice for this type of BR was not my own decision"	1.6 (.9)	1.3 (.6)	0.07
14. "In the decision-making process for this type of BR I was affected by my physician/plastic surgeon"	2.7 (1.4)	2.0 (1.1)	0.004

BR: breast reconstruction; DIEP: Deep Inferior Epigastric artery Perforator; SD: standard deviation * Mann-Whitney test, unless otherwise indicated; **: Fisher's exact test

Information concerning DIEP flap BR was less readily available ($p = 0.001$) and less clear ($p = .022$) than information regarding implant BR. Women opting for DIEP flap BR more actively sought for information ($p = 0.003$).

Women in both groups indicated they supported their decision, although there was a trend that women in the implant group had the feeling the choice for their type of BR had not entirely been their own ($p = 0.07$).

Autonomy and coping styles

Women from both BR groups did not significantly differ in self-awareness, the extent to which they are sensitive to others and their capacity to manage new situations. Their use of coping styles was also not significantly different (Table 3).

Table 3. Mean Autonomy and Coping styles subscale scores of implant and DIEP flap BR patients

	Implant group	DIEP-flap group	p Value*
	n = 71	n = 82	
	M (sd)	M (sd)	
Autonomy (ACS-30)			
Self-awareness	3.9 (.7)	3.9 (.7)	0.88**
Sensitivity to others	3.6 (.5)	3.5 (.6)	0.16
Capacity to manage new situations	3.1 (1.1)	3.2 (.9)	0.96
Coping styles (UCL)			
Active coping	19.8 (3.4)	20.0 (2.9)	0.64
Palliative reaction pattern	18.8 (3.5)	18.5 (3.3)	0.40
Avoidance and awaiting	15.7 (3.1)	15.5 (2.6)	0.76
Seeking social support	15.9 (3.5)	15.7 (3.8)	0.71
Passive reaction pattern	10.6 (2.7)	10.8 (2.5)	0.70**
Expressing emotions	6.3 (1.4)	6.5 (1.7)	0.58**
Comforting thoughts	13.6 (2.3)	13.4 (2.4)	0.56

Higher scores indicate more self-awareness, sensitivity to others, capacity to manage new situations, and more use of the coping styles. * Student t-test unless otherwise indicated; ** Mann-Whitney test; DIEP: Deep Inferior Epigastric artery Perforator; SD: standard deviation; ACS-30: Autonomy Connectedness Scale - 30; UCL: Utrecht Coping List

Comparing the ACS subscales with the normal population, our patients had significantly lower scores on the ACS subscale "Sensitivity to Others" ($t_{(241)} = 4.44$; $p < 0.001$) [29], meaning they are less sensitive to others opinions, wishes and needs and are less likely to adapt to another person's beliefs or preferences. They scored higher on the UCL subscales "Palliative Reaction Pattern" ($t_{(379)} = -2.99$; $p = 0.003$), "Seeking Social Support" ($t_{(289)} = -4.01$; $p < 0.001$) and "Comforting Thoughts" ($t_{(351)} = -5.77$; $p < 0.001$), indicating our patients more often try to relax, share their worries with others and try to have positive thoughts when they need to adapt to demanding situations, compared to the healthy population.

Determinants of active information seeking

Patients who scored higher on the Active Coping Scale, more actively sought for information regarding BR ($p = 0.02$). In addition, women opting for DIEP flap BR were more active information seekers ($p = 0.003$). Finally, we found a tendency towards a higher score on the

autonomy scale “Sensitivity to Others”, which was almost significantly associated with active information seeking ($p = 0.053$, Table 4), indicating that women who are more sensitive to others, tend to seek more actively for information regarding BR.

Table 4. Determinants for actively searching for information regarding BR (item 12) after 9 steps

	B	Std. Error	Beta	t	Sig.
Constant	0.71	0.92		0.76	0.45
Choosing implant (1) or DIEP flap BR (2)	0.53	0.17	0.24	3.02	0.003
Sensitivity to others (ACS-30)	0.32	0.16	0.16	1.95	0.05
Active coping (UCL)	0.07	0.03	0.19	2.36	0.02

BR: breast reconstruction; ACS-30: Autonomy Connectedness Scale; UCL: Utrecht Coping List; B: regression weight; Beta: standardized regression weight.

Discussion

In this study we explored information seeking behavior with regard to type of breast reconstruction in women, who were scheduled for either implant or DIEP flap BR after mastectomy.

Understandably, most women with therapeutic mastectomy combined with CPM were scheduled for implant BR (84%). Immediate bilateral BR with more complex reconstruction techniques like the DIEP flap method, is more difficult to schedule due to logistic problems because of limited availability and longer operation times resulting in long waiting lists. In addition, bilateral DIEP flap BR requires abdominal tissue for two flaps, which could have been a limitation for women with a lower BMI.

We found that 38% of women who had decided for implant BR were initially not aware of the option to reconstruct breasts with autologous tissue. The option of DIEP flap BR may not have been discussed with or offered to the patient because of insufficient abdominal tissue, due to logistic issues or the absence of required surgical expertise [35]. In addition, some women may have decided in favour of implant BR before they had their first consultation with the plastic surgeon. Information by the plastic surgeon on alternative options for BR may, therefore, not have altered their final decision.

Women in the implant group rated most information resources as less important than women in the DIEP flap group. Most women in the implant BR group had limited time to search for BR methods and perhaps less time to consult different resources as their time between mastectomy and BR was more often immediate or shorter compared to DIEP flap BR patients. Dealing with the diagnosis may have been their main priority instead of focusing on BR. Women opting for DIEP flap BR may have had more opportunity to think about their reconstruction options and to consult different resources. Eventually, this could have led to the decision to opt for a more complex BR method. We did not ask *why* they had a prolonged time between mastectomy and reconstruction.

The reconstructive surgeon was the most important resource for both groups. For women who opted for implant BR, their surgeon was of greater influence on their decision. We speculate that women scheduled for immediate BR, given the time pressure and expected higher distress, may have relied more on the surgeon than women who had more time to consider alternative BR options. In addition, plastic surgeons may have suggested to undergo implant BR in these cases as it is a relatively simple, obtainable and cheaper method. Obviously, their professional advice may also have been based on other patient-related factors.

Patients reported that information regarding DIEP flap BR was less clear and less readily available than information about implant BR. An explanation could be that DIEP flap BR is generally less obtainable and a more complex BR technique compared to the more commonly performed implant BR.

Active seeking for information about BR was associated with the decision to opt for DIEP flap BR and with an active coping style. In accordance with previous findings, patients who had chosen microsurgical DIEP flap BR were active information seekers compared to women who had opted for implant BR [25]. Active information seeking is obviously required to be comprehensively informed about reconstruction options as information regarding DIEP flap BR may generally not have been actively offered by all physicians and/or institutions. On the other hand, patients who were engaged to their decision for DIEP flap BR, may have searched more actively for information.

The study-specific questionnaire showed that women in the DIEP flap group were more independent in their decision for BR compared to women choosing implants, which is in concordance with the findings of the study of Matros et al. [25]. Although data from the autonomy questionnaire ACS-30 were not significantly correlated with the decision for the type of BR, the patients in our study were more independent in their decision-making compared to a healthy sample of Dutch women.

Furthermore, when comparing our patients' coping styles, we found they scored higher on the subscales "Palliative Reaction Pattern", "Seeking Social Support" and "Comforting Thoughts" than the normal Dutch population. These findings indicate that women choosing BR generally try to distract themselves more when they are worried, seek social support and think positive, compared to healthy women. This is in accordance with previous studies that have shown that women with early-stage BC and BC survivors often have more adaptive coping styles compared to healthy women, which is positively correlated with quality of life aspects and personal growth [36-39].

A limitation of the present study could be that more women planned for CPM chose to participate in our study compared to women with unilateral therapeutic mastectomy. Women with CPM were mostly diagnosed with BC in the past, and therefore, at the time of inclusion could possibly focus on BR and study participation, instead of having BC treatment as their priority. We do not think this affected the representation of our population, although we have to keep in mind participants may have been more committed to their decision regarding BR.

Inevitably, our study was limited by selection bias, as patients could not be randomized to the BR type they received. In addition, not all participating hospitals offered both BR types described. However, DIEP flap BR was carried out in one of the academic centers as well as in one of the general hospitals, suggesting it was offered to different populations. Although one could argue the present study should have been carried out in a selection of patients that had been offered identical reconstruction options, we believe a large group of patients from multiple centers is representative for the Dutch patient population as information provision regarding BR is currently not standardized in our country. This is probably true for other countries as information regarding BR seems not yet standardized [4;40].

In conclusion, women opting for DIEP flap BR were more active and independent in their decision-making regarding the type of BR. Women opting for implant BR seemed less well-informed and more dependent on their surgeon. Possibly the pool of women who had implant BR and who were mainly influenced by their surgeon, could have been convinced to have a DIEP flap BR. However, although the decision regarding the type of BR is ultimately the patient's, factors such as patient suitability for a procedure, risk factors and timing of BR play a role in reaching this final decision.

During patient consultation regarding treatment options by (reconstructive) surgeons, it is necessary to verify if the patient is aware of all her reconstruction possibilities, including the opportunity to delay BR. In addition, it is important to specifically ask for her own preferences and expectations, to increase the chance that she will receive the reconstruction that suits best with her needs and wishes that will eventually improve satisfaction [41].

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CHAPTER 4 THE SHORT-TERM PSYCHOLOGICAL IMPACT OF COMPLICATIONS AFTER BREAST RECONSTRUCTION

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Abstract

Objectives Few studies have focused on the psychological impact of postoperative complications after breast reconstruction (BR). As postoperative complications after BR usually lead to a prolonged recovery time and sometimes require additional surgery, the short-term impact on distress was investigated.

Methods Pre- and postoperatively, psychological questionnaires were sent to 152 women who underwent either implant BR (ImBR) or Deep Inferior Epigastric artery Perforator flap BR (DiepBR). In addition, patients and physicians reports of post-operative complications during the first 4 to 6 weeks after BR were scored. The course of anxiety, depression and cancer-specific distress and the effect of complications on distress were investigated.

Results ImBR patients reported decreased anxiety after surgery, and both groups reported reduced cancer-specific distress after surgery. However, depressive symptoms tended to increase after DiepBR. If complications occurred, both reconstruction groups reported increased depressive and anxiety symptoms, DiepBR patients even had depressive symptoms of clinical concern. A significant number of patients with complications reported alarming levels of distress. Timing and laterality were not significantly correlated with distress.

Conclusions Complications after BR have a significant impact on emotional well-being shortly after surgery. As distress affects quality of life and health outcomes, it is of great importance to offer psychological support to these patients. Distress can be evaluated by monitoring the emotional impact of BR during post-surgery consults, or with the standard use of short psychological questionnaires that patients can complete at home.

Introduction

Post mastectomy breast reconstruction (BR) for breast cancer can improve quality of life and patient satisfaction with the aesthetic result [1-4]. Unfortunately, most BR techniques have a considerable risk for complications [5-8], which could negatively affect psychosocial outcomes. Although many studies focused on psychosocial outcomes after BR, only very few have specifically focused on the psychological impact of complications after BR [9].

Implant BR can be performed either one-staged (direct insertion of prosthesis) or two-staged (insertion of tissue expander followed by replacement with definite implant). The overall short and long-term complication rates after implant BR vary from 18% to 51% [7;8;10-12]. Complications like infections, seroma and hematoma occur in between 15% to 39% of cases, of which 3% to 20% result in implant removal on short-term [8;11].

The short and long-term complication rates after autologous BR vary between 32% and 43% [6;7]. After Deep Inferior Epigastric artery Perforator (DIEP) flap BR immediate complications like hematoma, seroma and partial flap necrosis occur in about 2%, 5% and 15%, respectively [13]. In experienced hands total flap loss occurs in about 2% of DIEP flap reconstructions [14;15].

Factors such as the reconstruction method, type of prosthesis, and risk factors for wound healing problems such as obesity, smoking, hypertension and pre- or postoperative radiation therapy influence the chance for BR failure [11;16-18]. In particular, postoperative radiation therapy in patients with implant BR increases the complication risk, when compared to women with autologous BR [10;17]. For abdominal flap BR, the number of perforators included in the flap is also related to the occurrence of complications such as fat necrosis [19].

Women diagnosed with breast cancer can experience elevated stress levels around the time of surgery and prior to BR [20;21]. Pre-surgery distress has shown to contribute to post-surgery nausea, fatigue and discomfort [22]. In addition, postoperative complications may increase stress, which decreases the immune response and in turn may impede the healing process and increase the risk for infection [23;24].

We hypothesized that patients with complications after BR would experience increased psychological distress while recovering. To our knowledge, a prospective exploration of the relationship between psychological distress and postoperative complications after breast reconstructive surgery has not yet been performed. Exploring patients' emotional wellbeing after BR provides the opportunity to support them during an adverse recovery period, which may lead to better health and psychosocial outcomes. DIEP flap BR is a relatively new technique [25] of which the psychosocial effects have been less studied than the more often performed implant BR. Our main goal was to examine the relationship of short-term complications and psychological distress of women undergoing either implant or DIEP flap BR.

Patients and Methods

Patients

This study is part of a multi-centre prospective follow-up study on the psychological impact of BR. Participants were women who opted for post mastectomy reconstruction after breast cancer (unilateral or bilateral)². Reconstructions were either implant or DIEP flap based, and were immediate or delayed. All patients consented to participate in the study.

Exclusion criteria were a BR in the past, a detection of residue or metastasis of breast cancer, and not being able to understand and speak the Dutch language sufficiently. Women who did not consent or respond two weeks after the invitation were considered as non-respondents. Patients were approached between December 2007 and May 2010 at the Leiden University Medical Center (LUMC), Erasmus University Medical Center Rotterdam (EMCR), Daniel den Hoed Cancer Center, Haga Teaching Hospital, Rijnland Hospital Leiderdorp, the Lange Land Hospital, Hospital Walcheren, Oosterschelde Hospital and at the Hospital Zorgsaam. Ethics approval was obtained from all participating hospitals.

Implant BR

All 96 patients who were scheduled for implant BR (usually preceded by tissue expansion) were invited to participate in the study. Fifteen women did not respond, 10 patients declined and 71 women consented to participate (74%).

DIEP flap BR

All 100 women who were scheduled for a DIEP flap BR were asked to take part in the study. Seven women did not respond, 12 patients declined and 81 women consented to participate (81%).

Procedure

Preoperatively, 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. If patients did not respond within two weeks, a reminder was sent by letter or by phone if surgery was planned in the short term. Patients who returned informed consent received a questionnaire that they had to complete preoperatively. Postoperatively, patient-reported clinical data were confirmed by medical records. Four weeks post-surgery, patients completed same the questionnaire that was sent preoperatively and they were contacted by telephone to assess complications and pain levels.

Questionnaires

Demographic information (e.g. age, having a partner or children (at home), educational level), and clinical data (e.g. indication for mastectomy, body mass index (BMI)) were collected using self-report questionnaires.

² For 34 patients (31respondents) in addition to unilateral therapeutic mastectomy, contralateral prophylactic mastectomy was performed because of a BRCA1 or BRCA2 (13x) or unknown mutation (1x); a familial risk (6x); a high risk for developing breast cancer following treatment for Hodgkin's disease (3x); or for unknown reasons (11x).

Anxiety and Depression

Pre- and post-surgery, anxiety and depressive symptoms were measured with the Hospital Anxiety and Depression Scale (HADS) [26]. Questions to measure anxiety were, for example, “Do you worry a lot?”; “Do you feel something awful is about to happen?” and for depression: “Do you look forward with enjoyment to things?” and “Do you feel generally optimistic about the future?” Reported reliability and validity are sufficient [27;28]. The HADS uses a 4-point Likert scale and includes two subscales that measure anxiety and depression (each consists of 7 items). Both subscale scores range from 0 to 21. A score of 8 or above was used to indicate anxiety and depression of clinical concern [26;28], which we describe as patients with serious or alarming levels of distress.

Breast cancer specific distress

Pre- and postoperatively, cancer-specific distress (CSD) was measured using the Impact of Event Scale (IES), which includes 15 items [29;30]. The IES measures the extent to which one is overwhelmed by intrusive thoughts and avoidant behavior regarding a specific traumatic event, in this case breast cancer. Items can be scored as follows: 0 ‘not at all’, 1 ‘seldom’, 3 ‘sometimes’ and 5 ‘often’, for example: “I had trouble falling asleep or staying asleep, because of pictures or thoughts about breast cancer that came into my mind”. The total IES score is used in this study with a range from 0 to 75. Reported reliability and validity of the IES are satisfactory [29;31]. The categorization of the IES score is not indicative for specific clinical diagnoses, but a cutoff score of 20 or higher can be used to indicate high symptom levels [31;32].

Complications

A complication was defined as any adverse event which occurred during the first four to six weeks after surgery. A major complication was defined as an adverse event leading to a re-operation. A structured complication list was added to the medical records to inquire postoperative complications related to BR, which was filled in by the plastic surgeon and complemented by the data manager of the study. In addition, the list was completed by patients during post-surgery telephone contacts to measure self-reported complications. Patients were also asked to rate the average pain experienced from the immediate postoperative period until the time of the interview on a 10-point scale, with 1 indicating “no pain” and 10 indicating “extreme pain”. A numeric pain rating scale has been found to be a reliable and valid method [33;34]. A cutoff score equal to or higher than 4 was used to indicate serious pain.

Statistical analyses

Differences between implant and DIEP flap BR for dichotomous variables were analyzed with Fisher’s exact tests. Normally distributed continuous variables were analyzed using Student’s t-tests; for non-normally distributed variables transformed data were used. Ordinal variables were analyzed with Mann-Whitney tests. We corrected for demographic and clinical variables in which patient groups differed if a correlation of at least 0.24 with

the outcome variable was found [35]. Repeated-measures analysis of covariance (ANCOVA) was used for longitudinal analyses. Data were analyzed with the statistical package SPSS 17.0 (SPSS Inc., Chicago). Two-sided p-values < .05 were considered statistically significant.

Results

Non-respondents

Three non-respondents (7%) underwent a contralateral prophylactic mastectomy in addition to unilateral therapeutic mastectomy, compared to 31 respondents (20.4%; $p = 0.04$). Non-respondents and respondents did not significantly differ in age and timing of BR ($p = 0.50$ and $p = 0.35$, respectively).

Dropouts and lost to follow-up

One patient with diabetes mellitus died 18 days after DIEP flap BR due to unexpected sepsis as a result of pneumonia. Three patients who developed metastases during follow-up were excluded from analyses regarding distress: one patient's implant BR was postponed when skeletal, liver and kidney metastases were detected; in one DIEP flap patient a residue of breast cancer was detected during surgery; and one DIEP flap patient was diagnosed with skeletal metastases after BR. Furthermore, one woman withdrew from the study; three patients did not return the follow-up questionnaire and two patients refused telephone contact.

Demographic and clinical characteristics

A description of the patient characteristics in each reconstruction group is demonstrated in table 1.

Postoperative pain and complications

Telephone calls with 150 patients were performed on average 4.2 weeks after surgery ($sd=2.1$). Women with implant BR ($n=64$) reported a mean postoperative breast pain level of 4.3 ($sd=2.3$) compared to 2.4 ($sd=1.6$) after DIEP flap BR ($n=75$; $p < .001$). Furthermore, significantly more patients reported considerable pain symptoms (≥ 4) after implant BR ($n=37$; 58%) than after DIEP flap BR ($n=14$; 19%), $p < 0.001$. A mean abdominal pain level of 3.5 ($sd=2.3$) was reported by DIEP flap patients ($n=76$) and 42% indicated this pain level with 4 or higher.

More postoperative complications after DIEP flap BR (36%) than following implant BR (21%) were reported, following the surgeon reports, while patient-reports did not show differences in postoperative complications (46% and 35%, respectively). About 13% of patients from both groups had to be re-operated due to major complications within 6 weeks after the initial BR. Both patient groups reported the same rate of wound healing disturbances, however, more women tended to report wound dehiscence after DIEP flap surgery ($p=0.07$, Table 2). Finally, 11% of the implant BRs failed (tissue expander or implant was removed) and 6% of the patients with DIEP flap BR had either partial (5%) or total (1%) flap loss.

Table 1. Participant characteristics

	Implant group	DIEP flap group	p Value*
	n = 71 (%)	n = 81 (%)	
Mean age at time of breast reconstruction (sd)	49.1 (10.0)	49.3 (7.9)	0.90**
Having a partner	62 (87.3)	64 (79.0)	0.20
Having children	62 (87.3)	69 (85.2)	0.82
Having children at home	42 (59.2)	43 (53.1)	0.51
Education level			
low	15 (21.1)	16 (19.8)	
intermediate	27 (38.0)	28 (34.6)	0.59¶
high	29 (40.8)	37 (45.7)	
Inherited predisposition for BC ^a	21 (29.6)	17 (21.0)	0.26
Laterality			
Unilateral BR	43 (60.6)	70 (86.4)	< 0.001
Bilateral BR	28 (39.4)	11 (13.6)	
BR Timing			
Immediate BR	43 (60.6)	2 (2.5)	
Delayed BR	15 (21.1)	75 (92.6)	
Immediate + delayed BR	13 (18.3)	4 (4.9)	< 0.001***
Mean time since mastectomy in years (sd)	1.4 (3.6)	3.2 (2.6)	< 0.001¶
Mean BMI (sd)	24.1 (4.1)	27.6 (3.7)	< 0.001**
Chemotherapy prior to BR	18 (25.4)	57 (70.4)	< 0.001
Radiation therapy prior to BR	10 (14.1)	28 (34.6)	0.005
Chemotherapy after BR	12 (16.9)	1 (1.2)	< 0.001
Radiation therapy after BR	5 (7.8)	1 (1.2)	0.02

^a: brca1/brca2/familial risk; BC: breast cancer; BMI: body mass index; DIEP: Deep Inferior Epigastric artery Perforator; SD: standard deviation; * Fisher's exact test unless otherwise indicated; ** Student's t-test; *** Chi-Square test; ¶ Mann-Whitney test.

Pre- and postoperative anxiety, depression and cancer-related distress

After implant BR, patients reported a decline in anxiety and cancer-related distress ($p=0.04$ and $p < 0.001$, respectively, Table 3). Their depression scores did not significantly change. Women with DIEP flap BR reported a slight increase in depressive symptoms, but significantly less cancer-related distress after surgery than before surgery ($p=0.09$ and $p < 0.001$, respectively). However, their anxiety symptoms did not change significantly over time (Table 3).

Patients who were about to undergo implant BR experienced more CSD preoperatively, but the reconstruction groups did not significantly differ in anxiety and depression symptoms ($p=0.007$, $p=0.13$ and $p=0.59$, respectively). Post-surgery scores of anxiety, depression and cancer-related distress did not differ between the patients who underwent implant and those who underwent DIEP flap surgery ($p=0.51$, $p=0.92$ and $p=0.11$, respectively).

Table 2. Type of self-reported complications

	Implant Group	DIEP flap Group	p Value*
	n = 66 (%)	n = 79 (%)	
<i>Major complications (leading to re-operation)**</i>	9 (13.6)	11 (13.9)	1.00
<i>Wound healing complications</i>			
Wound dehiscence	6 (9.1)	16 (20.3)	0.07
Wound infection	10 (15.2)	14 (17.7)	0.82
Haemorrhage (bleeding)	4 (6.1)	2 (2.5)	0.41
Hematoma	1 (1.5)	3 (3.8)	0.63
Fat necrosis	0	2 (2.5)	0.50
Skin necrosis	2 (3.0)	4 (5.1)	0.69
Seroma	3 (4.5)	3 (3.8)	1.00
Spitting of resorbable stitches	1 (1.5)	0	0.46
<i>Implant-related complications</i>			
Tissue expander/implant removal	7 (10.6)		-
<i>Flap complications</i>			
Partial flap loss		4 (5.1)	-
Total flap loss		2 (2.5)	-
Circulation problems flap		13 (16.5)	-
<i>General complications</i>			
Painful arm	0	1 (1.3)	1.00
Symptomatic pulmonary embolism	0	2 (2.5)	0.50
Pneumonia	0	2 (2.5)	0.50

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

** Re-operations due to wound dehiscence and/or infection (n = 6), haemorrhage (n = 6), skin necrosis (n = 3), circulation problems flap (n = 5) and seroma (n = 1)

Table 3. Pre- and postoperative distress scores of women undergoing BR

	Implant BR				DIEP flap BR				p Value*
	Preoperative		Postoperative		Preoperative		Postoperative		
	N	M (sd)	M	(sd)	N	M (sd)	M	(sd)	
Anxiety (0-2) ¹ a	67	5.6 (4.0)	4.6 (3.5)		77	4.6 (4.1)	4.2 (3.8)		.35
Depression (0-21) ^a	67	5.4 (3.6)	6.2 (4.6)		77	5.1 (3.7)	6.5 (5.4)		.09
Cancer-specific distress (0-75) ^b	65	26.0 (13.7)	19.2 (13.6)		76	19.9 (12.6)	15.9 (12.8)		<.001

DIEP: Deep Inferior Epigastric artery Perforator; BR: breast reconstruction; M: mean; sd: standard deviation; * Student's t-test on transformed data; ^aHADS: Hospital Anxiety and Depression Scale, higher scores mean higher anxiety and depression levels; ^bIES: Impact of Event Scale, higher scores mean higher distress levels.

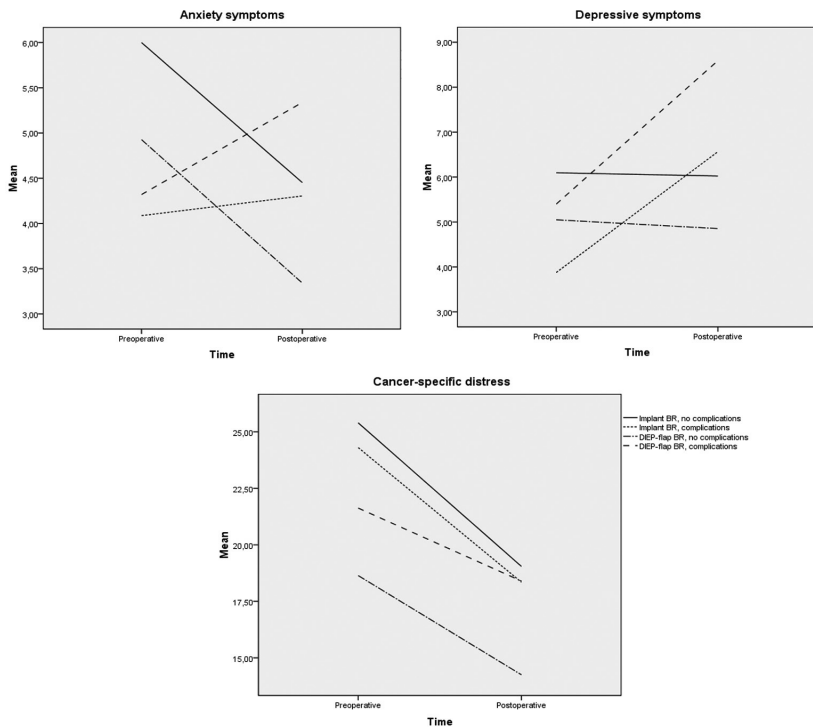
**The effect of complications on anxiety, depression and cancer-specific distress
Covariates**

The correlation of different clinical variables with distress was explored to identify covariates. Pre-surgery anxiety and CSD were significantly related to breast pain ($r=0.27, p=0.001$ and $r=0.28, p=0.001$, respectively), indicating that patients who felt more anxious and had more CSD before surgery experienced more pain after BR. Post-surgery CSD was related to chemotherapy after surgery and breast pain ($r=0.24, p=0.003$ and $r=0.25, p=0.003$, respectively), indicating increased symptoms of CSD were associated with more pain and undergoing chemotherapy after surgery.

The variable ‘self-reported complications’ was not significantly related to the clinical variables (including breast pain) indicating that this was an independent measure. Self-reported complications for each patient correlated strongly with surgeon-reported complications for each patient ($r=0.56, p < .001$), demonstrating that the reported complications concerned generally the same patients. Other characteristics, such as laterality and timing of BR had no significant relation with anxiety, depression and CSD.

To analyze the effect of complications on the course of anxiety, depression and cancer-related distress, we corrected for ‘breast pain’ and ‘postoperative chemotherapy’, if relevant.

Figure 1. The course of anxiety, depression and cancer-specific distress symptoms if complications were reported after implant or DIEP flap breast reconstruction



Anxiety

Correcting for breast pain, the course of anxiety was significantly related to complications $F(1, 130)=5.29, p=0.02$, indicating that patients who experienced complications had increased anxiety symptoms after surgery compared to patients not reporting complications. Additionally, a significant interaction effect between the type of BR and complications was found, $F(1, 130)=7.28, p=0.02$, demonstrating that patients with DIEP flap BR experienced a greater increase of anxiety after surgery when reporting complications (Figure 1).

Depression

Depression was also significantly related to complications $F(1, 137)=11.74, p=0.001$, indicating that patients who reported complications had more depressive symptoms after surgery than patients without self-reported complications. Between-subjects effects showed an interaction between the type of BR and complications $F(1, 137)=5.59, p=0.02$, indicating that DIEP flap patients felt more depressed after surgery if complications occurred (Figure 1).

Cancer-specific distress

Correcting for 'breast pain' and 'post-surgery chemotherapy,' the course of CSD was not significantly related to complications $F(1, 127)=0.75, p=0.39$. No interaction effect was found in type of BR and complications $F(1, 127)=0.70, p=0.40$, demonstrating that both reconstruction groups reported decreased CSD symptoms independent of experiencing complications (Figure 1).

Occurrence of disturbing levels of distress after experiencing complications

Of the women reporting post-surgery complications after implant BR, 13%, 39% and 44% reported anxiety, depression and cancer-related distress of clinical concern, respectively (Table 4). Of the women with complications following DIEP flap BR, 31%, 49% and 40% reported alarming levels of anxiety, depression and cancer-related distress, respectively, after surgery.

Table 4. Occurrence of disturbing levels of anxiety, depression, and cancer-related distress, preoperatively and after experiencing postoperative complications

	Implant BR		DIEP flap BR	
	n = 23		n = 35	
	T0	T1	T0	T1
Anxiety ^a ≥ 8	17%	13%	11%	31%
Depression ^a ≥ 8	17%	39%	17%	49%
Cancer-specific distress ^b ≥ 20	61%	44%	51%	40%

DIEP: Deep Inferior Epigastric artery Perforator; BR: breast reconstruction; M: mean; SD: standard deviation; ^aHADS: Hospital Anxiety and Depression Scale, higher scores mean higher anxiety and depression levels; ^bIES: Impact of Event Scale, higher scores mean higher distress levels. T0 = prior to surgery, T1 = after surgery

Discussion

In this study we prospectively explored the relationship between psychological distress and short-term complications after BR in women who underwent either implant or DIEP flap BR following mastectomy. As the two reconstruction groups were pre-selected and as they differ in important clinical characteristics, they theoretically cannot be compared. The patient groups are, nevertheless, representative for the Dutch population, as we recruited patients from different areas in the Netherlands. We should bear in mind that BR should be tailored to the needs of the patient. We will provide further clarification to explain the clinical differences between the two reconstruction groups and their possible influences on distress.

It is understandable that more women scheduled for immediate and bilateral BR underwent implant BR. Immediate bilateral BR with more complex methods such as a DIEP flap is difficult to schedule due to logistic problems, such as long operation times resulting in prolonged waiting lists. In addition, bilateral DIEP flap BR requires abdominal tissue for two flaps, which could have been a limitation for women in the implant group having a lower mean BMI. However, the timing and laterality of BR were not significantly correlated with the psychological outcomes, nor with the complication rate.

In congruence with previous findings, patients with DIEP flap BR had a relatively high BMI [36;37]. This could have affected the complication rate [10]. Although more DIEP flap patients had undergone chemo- and radiation therapy prior to BR, this does not seem to be a risk factor for major complications in autologous BR [10]. However, more women in the implant group received chemo- and radiation therapy after BR, which might have increased their complication rate [17]. Other risk factors might have played a role in the occurrence of complications in both groups; however, this study focused on the *psychological impact* of complications.

Patients with implant BR reported serious breast pain which is not surprisingly as the tissue expander or prosthesis is subpectorally placed [38]. Women with DIEP flap BR experienced more abdominal than breast pain, as a result of abdominal tightness after closure of the DIEP flap donor-site. Although we did not structurally assess pain management after surgery, their lower mean pain scores are probably related to the standardized pain management after DIEP flap BR, consisting of a patient-controlled analgesia pump followed by conversion to oral narcotics [39].

Interestingly, more patients reported complications compared to the surgeon-reports. Based on the surgeon-reports, more patients in the DIEP flap group had postoperative complications compared to women with implant BR. It is possible that not all (minor) complications were registered in the medical records. On the other hand, patients may have a subjective perception of complications, which could have led to an increased self-reported complication rate. However, as we focused on patients' quality of life, we assumed their own perception was of greater relevance. The total self-reported complication rate did not significantly differ between women who underwent either implant or DIEP flap BR, which is congruent with current literature [10].

Preoperatively, women scheduled for implant BR even had CSD levels of clinical concern (> 20). This can be explained by the fact that most of the implant BR patients were about to have immediate BR and were awaiting mastectomy. As a consequence of a recent breast cancer diagnosis they were still in the emotional rollercoaster of the treatment. After surgery anxiety and CSD decreased in congruence with earlier findings [40]. CSD also decreased in DIEP flap BR patients, who showed lower preoperative scores, possibly because the majority was already cured from cancer. However, timing of BR was not significantly correlated to distress. Therefore, a more plausible explanation for higher preoperative scores in the implant group, could be that more anxious women tended to choose for implant BR, as this type of surgery seems less intimidating than DIEP flap BR. Post-surgery, depressive symptoms slightly increased in women who had DIEP flap BR. An explanation would be the heavy physical burden of DIEP flap BR which can be very intense, as it additionally includes recovery from abdominoplasty.

Patients reporting complications had increased anxiety and depressive levels, particularly, DIEP flap patients who even reported critical depression levels. Serious complications after DIEP flap BR, such as flap circulation problems, can lead to immediate partial or total flap loss which may be physically as well as psychologically threatening. Common complications occurring after implant BR, such as minor wound infections, could, in contrast, resolve more easily and do not necessarily lead to immediate expander/implant loss, which may be less psychologically challenging. Increased distress after having complications after BR, is comparable with inclined distress after recovering from mastectomy with complications, perhaps indicating recovery from BR reminds patients of mastectomy [41]. However, CSD decreased, as women were possibly relieved that surgery had passed, and that possible cancer risks declined if they also underwent mastectomy.

It remains important to differentiate between the psychological effect of minor versus major complications, as the latter may lead to more psychological disturbances. However, the sample size limits the power for more detailed subgroup analyses, and therefore we recommend including more patients in future studies.

The aesthetic outcome directly after BR could have also influenced psychological wellbeing, as in the immediate postoperative period an aesthetic *end result* had not yet been reached. Particularly for the women who had received a tissue expander in the implant group. Body image and aesthetic satisfaction could be diminished immediately post-surgery, which could negatively impact distress. We did not measure body image or aesthetic satisfaction at this point, which may be a limitation of the present study. Postoperative radiation therapy (PRT) could have also influenced body image and aesthetic satisfaction and therefore, distress, but PRT was not significantly correlated with distress ($r < 0.09$). As PRT generally started within six weeks after surgery, its effect may not have been as damaging yet. Nevertheless, the small number of patients that had PRT may limit the detection of a statistically significant difference.

Significant proportions of women with complications after BR reported critical distress, particularly patients with DIEP flap BR. However, the actual chance for partial or total flap failure is lower compared to implant loss [8;11;13-15]. To identify *clinical cases* of anxiety and

depression a cut off score of 11 is recommended [26;28]. Post hoc analyses demonstrated that 9% of the implant group and 11% of the DIEP flap group had *clinical* anxiety after complications. However, still considerable proportions (implant BR: 22%; DIEP flap BR: 40%) had *clinical* depression levels after surgery if complications occurred.

In conclusion, although BR can improve quality of life, patients may experience significant distress immediately before surgery. After surgery, patients with complications report high levels of distress, especially DIEP flap BR patients. A significant number of women with complications experienced serious levels of anxiety, depression and CSD post-surgery. Although the present study included only the immediate postoperative period, it suggests that some patients may need more attention or even clinical referral for coping with distress while recovering from BR. In particular, post-operative distress may predict poorer longer-term psychosocial outcomes while better early post-operative outcomes may predict resilience to distress [42;43]. This hypothesis will be studied in our follow-up study of wellbeing one year after BR.

In practice, preoperatively patients should be clearly informed about the consequences of direct postoperative complications on mood and stress levels. They can be reassured that these feelings are not uncommon. Plastic surgeons and mamma-care nurses can specifically ask during pre- and post-surgery consults or surveillance how patients are feeling. Levels of distress especially need to be monitored in patients with complications, for example by completing a short distress-questionnaire like the HADS, which can be returned by mail to the nurse. In case of clinical concern, psychological referral is recommended to better cope with pre- and post-surgery distress. This may positively affect quality of life as well as health since distress could negatively affect the immune system as well as wound healing [23;24;44].

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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

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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 Zorgzaam 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 led 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%, $p=0.013$).

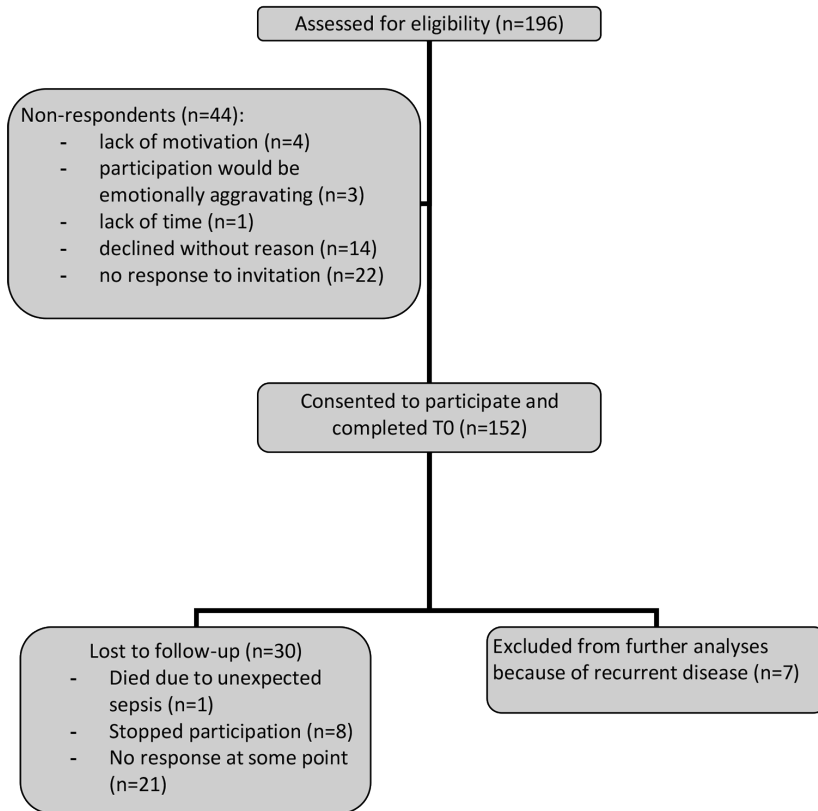
Patient characteristics and complications were reported for all participants fulfilling the inclusion criteria ($n=145$, Tables 1 and 2). Further analyses were performed on their data of all three assessments (T0: $n=145$; T1: $n=139$; T2: $n=119$, Tables 3 and 4).

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 (<i>sd</i>)	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 (<i>sd</i>)	2.3 (3.3)
Mean BMI in kg/m ² (<i>sd</i>)	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 (%)	
<u>One or more complications</u>	32 (45.7)	30 (40.0)	0.51
<u>Subsequent surgery for complications</u>	28 (40.0)	22 (29.3)	0.22
<u>Subsequent surgery more than once</u>	14 (20.0)	8 (10.7)	0.16
<u>Complete failure of BR</u>	9 (12.9)	1 (1.3)	0.007
<u>Type of complications</u>			
<u>Wound healing complications</u>			
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
<u>Implant-related complications</u>			
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)		
<u>Flap-related complications</u>			
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)	
<u>General complications</u>			
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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CHAPTER 6 IMPACT OF DELAYED IMPLANT AND DIEP FLAP BREAST RECONSTRUCTION ON BODY IMAGE AND SEXUAL SATISFACTION: A PROSPECTIVE FOLLOW-UP STUDY

Revision submitted

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Abstract

Objective Prospective studies regarding the psychosexual impact after different types of breast reconstruction (BR) are scarce. The impact of either implant or DIEP flap BR on body image and sexual relationship satisfaction was investigated in time.

Methods At baseline 98 women opting for delayed implant or DIEP flap BR after mastectomy for breast cancer completed a survey. The majority was followed up at 6 and 20 months postoperatively. Questionnaires included the Body Image Scale, Dutch Relationship Questionnaire, Short Form – 36 Healthy Survey and the Impact of Event Scale.

Results Mixed modeling analyses indicated that preoperative body image improved significantly after 20 months (Cohen's $d=1.51$, $p<0.001$) and there was no statistically significant difference between the two types of BR. A better body image was related to a better general mental health ($d=0.19$; $p=0.02$), less cancer distress ($d=-0.33$, $p<0.001$) and a higher partner relationship satisfaction ($d=0.27$, $p<0.001$). Sexual relationship satisfaction also increased after 20 months ($d=0.22$, $p=0.01$) and was positively related to more partner relationship satisfaction but negatively affected by hormonal therapy.

Conclusions Body image and sexual relationship satisfaction significantly improved after BR and this was not related to the BR type. Psychosexual consequences from previous cancer treatment may interfere. During the course of BR, extra attention should be paid to patients with lower general mental health, higher cancer distress, less partner relationship satisfaction or those with hormonal therapy as this can negatively affect body image or sexual relationship satisfaction.

Introduction

Psychosexual changes after breast cancer treatment include fear of loss of fertility, negative body image, loss of femininity and attractiveness, depression and anxiety [1-4]. A range of sexual complaints, such as dyspareunia, vaginal dryness, decreased sexual desire and/or sexual pleasure and numbness of the breasts, have been reported as a consequence of breast cancer treatment [5-13].

Generally, no differences have been found in body image and sexual satisfaction between women with breast-conserving therapy, mastectomy only, or mastectomy with breast reconstruction (BR), however, conflicting results have been reported [14-16]. This discrepancy suggests that different factors play a role in satisfaction with body image and sexuality after BR: direct and indirect effects of surgery, radiation, chemo- and hormonal therapy, as well as lowered physical and mental functionalities [5-13].

Several BR options exist after mastectomy: immediate as well as delayed reconstruction with implants, autologous tissue, or a combination of both [17]. The deep inferior epigastric artery perforator (DIEP) flap is a relatively new technique using abdominal tissue generally leading to high patient satisfaction [18;19] as well as more positive body image compared to implant BR [20-23].

As multiple factors affect outcomes after breast surgery, it is important to prospectively investigate these aspects in homogenous groups. The primary aim of this study was to *prospectively* investigate the impact of delayed implant and DIEP flap BR on body image and sexual satisfaction, which to the best of our knowledge has never been done by others [21;23;24]. Secondly, to study whether other clinical and psychological variables, were significantly related to changes in body image and/or sexual satisfaction.

Patients and Methods

Patients

This study is part of a multi-center prospective follow-up study on the psychological impact of BR [25-27]. For the current study, women opting for a delayed BR after a history of breast cancer were included. Some women also underwent a contralateral prophylactic mastectomy followed by bilateral reconstruction. Reconstructions were either implant based usually preceded by tissue expansion or using an artery DIEP flap³ from the abdomen [18].

Exclusion criteria were a previous BR, detection of recurrent loco regional or distant disease, and not being able to understand and speak the Dutch language sufficiently. Women who did not consent or who did not react two weeks after the invitation were considered as non-respondents. Patients were approached between December 2007 and May 2010 and ethics approval was obtained from all participating hospitals⁴. Of the 131 invited patients who were scheduled for delayed BR, 105 women (80%) consented to participate (Figure 1).

³ DIEP flap was performed only at Erasmus University Medical Center Rotterdam (EMCR) and the Haga Teaching (Haga) Hospital

⁴ Leiden University Medical Center (LUMC), EMCR/Daniel den Hoed Cancer Centre, Haga Hospital, Rijnland Hospital Leiderdorp, Hospital Walcheren, Admiraal de Ruyter Hospital Goes and at the Hospital Zorgsaam.

Procedure

Preoperatively, 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. A reminder was sent by letter if patients did not respond within two weeks or they received a reminder by phone if surgery was planned on short term. Patients, who returned informed consent, received the survey including a range of demographic, clinical and psychological questionnaires which they were requested to complete preoperatively (T0). Six months postoperatively (T1), patients filled in the same survey they previously had completed. Finally, the survey was sent after finishing the complete BR course, including nipple reconstruction if this was planned within the duration period of the study (T2). Women, who had not completely finished their BR course, completed the questionnaires regarding the preliminary end result.

Measurements

Demographic information (e.g., age, having a partner or children (at home), educational level), and clinical data (e.g., timing of BR, body mass index (BMI)) were collected in the survey and clinical data were confirmed by checking medical records. The following questionnaires had to be completed for at least 75% of the items to calculate scale scores.

Primary outcome measures

Body image

A study-specific body image scale (BIS) was developed (Appendix 1), based on Lodder et al [28], and is described elsewhere [29]. The scale consisted of 13 items which were scored from 1-5 (totally disagree, disagree, neutral, agree, totally agree, respectively). After recoding the negative items (items 4, 5, 11, 13), a mean scale score was calculated (1-5) where a higher score indicates a more positive body image. The internal consistency of the BIS was high in the current study sample (Cronbach's $\alpha = 0.89$). Two items were only completed by patients with a partner, nevertheless, for the single women a mean scale score was calculated as well as at least 75% (10 items) had to be completed.

Sexual relationship satisfaction

To investigate the course of satisfaction with the *sexual relationship*, the subscale 'sexuality' of The Dutch Relationship Questionnaire (NRV) was used [30]. The NRV has shown good psychometric properties and a total score on the subscale 'sexuality' below eight (range 0-12) indicates below average or low sexual relationship satisfaction and a bad sexual compatibility with the partner [30]. The NRV was completed only by women with a partner.

Secondary outcome measures

Satisfaction with the overall *partner relationship* was investigated with the NRV as well. Normally, the total score of the NRV can be used to provide this satisfaction score. However, to correct for the impact of sexual satisfaction, the score of the 'sexuality' subscale was

subtracted from the total score. Therefore, scores under 49 (range 0-68) indicate below average or low satisfaction with the partner relationship, excluding sexual satisfaction.

Breast cancer specific distress was measured using the 15-items Impact of Event Scale (IES) [31;32]. The total IES score was used in this study ranging from 0 to 75. Reported reliability and validity of the IES are satisfactory [31;33]. The categorization of the IES score is not indicative for specific clinical diagnoses, but a cutoff score of 20 or higher can be used to indicate high symptom levels [33;34].

Changes between baseline and follow-up measurements of *general mental and physical health* were assessed with the Dutch version of the 36-item Short-Form Health Survey (SF-36), designed to measure health related quality of life. General physical and mental complaints were measured with the Physical Component Summary (PCS) and the Mental Component Summary (MCS) of the SF-36, respectively [35-37]. These scales are aggregated from 8 subscales of the SF-36: physical functioning, social functioning, role limitations caused by physical health problems, role limitations caused by emotional problems, mental health, vitality, bodily pain and general health perception. In this norm based scoring method each scale has the same mean value (50) and standard deviation (10). Consequently, a scale score below 50 indicates a health status below average [36].

Statistical analyses

Descriptive statistics were calculated for all variables. Differences between respondents and non-respondents and between implant and DIEP flap BR patients were investigated using Student's t-tests, Mann-Whitney U tests and Fisher's Exact tests.

To investigate changes in time in the primary psychological outcome measures (body image and sexual satisfaction) after implant and DIEP flap BR, multi-level regression analyses (MLA) were performed, which can handle incomplete time-series data efficiently with a minimal loss of information. These analyses also compensate for different numbers of participants within the subgroups, and for dropout when dropout is dependent on variables that are included in the regression model [38].

Saturated models were postulated with time, time squared and relevant covariates. The time variable was coded 0, 6 and 20, respecting the uneven time spans between the measurements. The number of covariates in the models is limited by the number of participants and repeated measures. The number of 98 participants is sufficient for the determination of 6 medium sized covariates [39]. This is a conservative calculation, the three repeated measures allow for more covariates.

In a first step we reduced the number of relevant potential covariates, by calculating Spearman's correlation coefficients with all clinical pretreatment characteristics (Table 1) and changes in the psychological outcomes between baseline and 20 months (partner relationship satisfaction, cancer distress, general mental and physical health and body image or sexual satisfaction). Secondly, the variables that significantly correlated with change in the primary outcomes ($p < 0.05$), were entered in the multi-level regression analysis as covariates. Continuous covariates (age, cancer distress, general mental health) were centred for ease of interpretation. In this way the intercept indicates the estimated

value for a woman at the mean of the covariates. Changes in the secondary outcomes were investigated with separate MLA for each outcome measure including time effects only.

In a backward procedure all non-significant effects were removed from the model (p -out > 0.05), until a parsimonious model was reached. Effect sizes (Cohen's d) were calculated by dividing the difference between the follow-up estimates and baseline by the estimated standard deviation. An effect size of 0.20 was considered small, 0.50 medium and 0.80 large [40]. Two-sided p -values < 0.05 were considered statistically significant. Version 20 of IBM-SPSS Statistics (SPSS Inc., Chicago) was used for statistical analyses.

Results

Non-respondents

Non-respondents ($n = 26$) and respondents ($n = 105$) did not significantly differ in age, laterality and type of BR and therefore, we presumed the respondents were representative for the total group ($t(131)=0.026$, $p=0.98$; Fisher's Exact test's: $p=0.28$ and $p=1.00$, respectively).

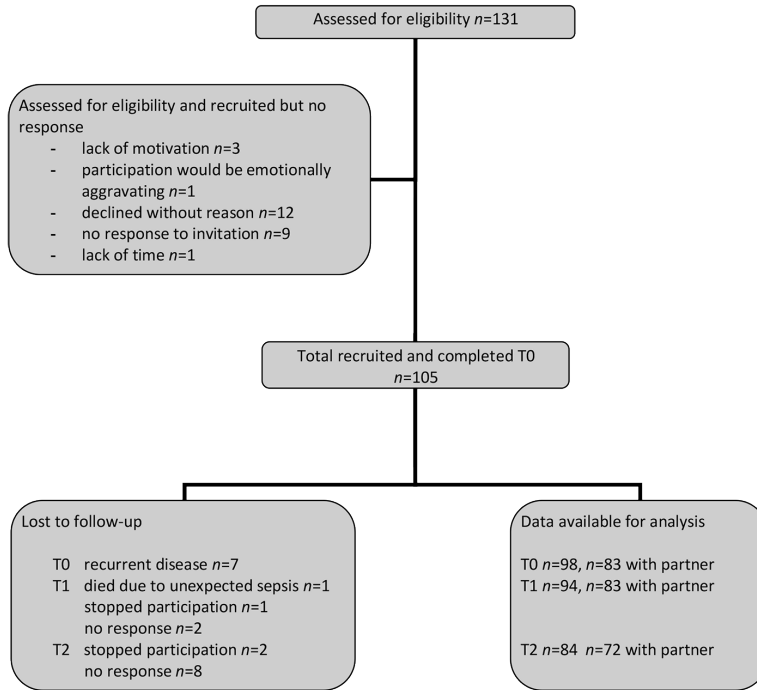
Lost to follow-up

Seven of the 105 women were excluded from analyses due to the development of metastases or recurrent disease (Figure 1), leaving 98 women for analyses at T0. Furthermore, one patient with diabetes mellitus died 18 days after DIEP flap BR due to unexpected sepsis as a result of pneumonia, one woman stopped participation at T1, and two women did not return the questionnaire at T1, leaving 94 women for analyses at T1. At T2, two women stopped participation and 8 participants did not return the questionnaire, leaving 84 women for analyses. These dropouts ($n=21$) did not differ significantly from the patients participating at T2 ($n=84$) regarding demographic variables (data not shown). However, dropouts had a significantly lower baseline general mental health ($p=0.026$). Analyses were performed on data of the 98 participants. The NRV was completed only by participants with a partner, and partner status did not significantly change during the study ($\text{Chi}^2=0.54$, $p=0.76$, Figure 1). Furthermore, occasionally not every questionnaire was totally completed, which explains different sample sizes per outcome.

Demographic and clinical characteristics

In both reconstruction type groups, patients had a mean age of 49 year. Twenty-two patients had an increased risk for developing breast cancer due to an inherited predisposition for BC (Table 1). Time since mastectomy was longer for DIEP flap BR patients compared to implant BR patients. More women with bilateral mastectomy received implant BR than DIEP flap BR. Women opting for DIEP flap BR had a higher mean BMI compared to women receiving implant BR. There were no significant changes in baseline psychological scores between women with either implant or DIEP flap BR.

[insert Table 1 about here]

Figure 1. Flow chart of patient inclusion

Changes in pre- and postoperative body image and sexual satisfaction

Body image

In the first step, Spearman's correlation coefficients revealed that age ($r=0.24$, $p<0.001$), mental health ($r=0.39$, $p<0.001$), sexual ($r=0.25$, $p<0.001$) and partner relationship satisfaction ($r=0.37$, $p<0.001$) as well as cancer distress ($r=-0.31$, $p<0.001$) were significantly correlated with change in body image. Consequently, these variables with body image time interactions were entered into the saturated multi-level models.

For body image a significant linear and a quadratic time effect was found (Table 2). These indicate a body image after 6 months of 3.74 ($3.0425 + 6*0.1481 - 36*0.0053=3.74$), an improvement of 0.70 ($d=1.24$, $p<0.001$, Table 3). After 20 months an improvement of 0.85 was found compared to baseline ($d=1.51$, $p<0.001$). No significant relationship was detected with the type of BR ($p=0.55$).

The final model for body image (Table 2) also indicated that a higher partner relationship satisfaction, less cancer distress, and a better general mental health were positively significantly related to a better body image of which the estimates, p -values and effect sizes are again demonstrated in Table 3. Age and sexual relationship satisfaction were not significantly related to body image ($p=0.068$ and $p=0.21$ respectively) and were therefore removed from the model.

Table 1. Baseline characteristics of 98 women with either a delayed implant or DIEP flap breast reconstruction after mastectomy for breast cancer

	Implant BR	DIEP-flap BR	<i>p</i> -value [^]
	N=25	N=73	
Mean age at time of breast reconstruction (sd)	48.7 (9.2)	49.4 (7.9)	0.73 ^{^^}
Mean years since mastectomy (sd)	2.9 (4.1)	3.2 (2.7)	0.03 ^{^^}
Having a partner (%)	24 (96.0)	59 (80.8)	0.11
Having children (%)	23 (92.0)	63 (86.3)	0.73
Education level			
low	6 (24.0)	11 (15.1)	
intermediate	7 (28.0)	28 (38.4)	
high	12 (48.0)	34 (46.6)	0.77 ^{^^^}
Inherited predisposition for BC ^a	7 (28.0)	15 (20.5)	0.58
Laterality			
Unilateral M+BR because of BC	13 (52.0)	62 (84.9)	0.002
Bilateral M+BR because of BC	4 (16.0)	4 (5.5)	0.20
Immediate contralateral prophylactic M+BR	8 (32.0)	7 (9.6)	0.02
Mean BMI (sd)	24.8 (4.4)	27.5 (3.6)	0.004 ^{^^}
Radiation therapy	13 (52.0)	49 (67.1)	0.23
Chemotherapy therapy	6 (24.0)	24 (32.9)	0.46
Hormonal therapy	8 (32.0)	40 (54.8)	0.06
Body image (1-5)	3.0 (0.8)	3.0 (0.7)	0.63 ^{^^}
Sexual relationship satisfaction (0-12)	8.8 (3.1)	7.3 (3.3)	0.07 ^{^^}
Partner relationship satisfaction (0-68)	58.0 (8.7)	57.7 (8.6)	0.88 ^{^^}
Cancer distress (0-75)	25.2 (15.4)	19.5 (12.6)	0.12 ^{^^}
General mental health	49.8 (10.5)	49.7 (10.5)	0.96 ^{^^}
General physical health	55.0 (6.7)	52.8 (8.7)	0.28 ^{^^}

^a: brca1/brca2/familial risk; M: mastectomy; BC: breast cancer; BMI: body mass index; DIEP: Deep Inferior Epigastric artery Perforator; BR: breast reconstruction; SD: standard deviation [^] Fisher's Exact test, unless indicated otherwise; ^{^^} Student's t-test (on transformed data for time since mastectomy and cancer distress); ^{^^^} Mann-Whitney U test.

Sexual relationship satisfaction

In the first step, correlation coefficients with potential covariates revealed significant relations with age ($r=0.13$, $p=0.04$), having had radiotherapy ($r=-0.16$, $p=0.018$) and hormonal therapy ($r=-0.18$, $p=0.006$), general mental health ($r=0.27$, $p<0.001$), the partner relationship satisfaction ($r=0.55$, $p<0.001$) and body image ($r=0.25$, $p<0.001$).

Satisfaction with the sexual relationship improved significantly in time ($d=0.22$, $p=0.010$ after 20 months, Table 3). Having had hormonal therapy was negatively related ($d=-0.51$, $p=0.012$) and partner relationship satisfaction ($d=0.54$, $p<0.001$) was positively related to sexual relationship satisfaction. The observed baseline effect of the type of BR presented in Table 1 ($d=.049$ $p=0.001$), indicating that women with DIEP flap BR were less satisfied with their sexual relationship, was not significant in the MLA ($p=0.085$).

Table 2. Changes in primary and secondary outcomes and covariates

	Estimate [95% CI]	Std. Error	p-value
Body image			
Intercept	3.0425 [2.2917 – 3.1684]	0.06380	< 0.001
Time	0.1481 [0.1152 – 0.1811]	0.01662	< 0.001
Time squared	-0.0053 [-0.0068 – -0.0038]	0.00077	< 0.001
Partner relationship satisfaction	0.0178 [0.0079 – 0.0276]	0.00499	< 0.001
Cancer distress	-0.0141 [-0.0204 – -0.0077]	0.00320	< 0.001
General mental health	0.0104 [0.0017 – 0.0190]	0.00440	0.019
Sexual relationship satisfaction			
Intercept	8.483 [7.700 – 9.266]	0.3944	< 0.001
Time	0.031 [0.0077 – 0.055]	0.0120	0.010
Hormonal therapy	-1.473 [-2.614 – -0.332]	0.5739	0.012
Partner relationship satisfaction	0.187 [0.146 – 0.228]	0.0210	<0.001
Cancer distress			
Intercept	20.384 [17.813 – 22.954]	1.2986	< 0.001
Time	-0.2428 [-0.3557 – -0.1299]	0.0572	< 0.001
General physical health			
Intercept	53.275 [51.660 – 54.890]	0.8177	< 0.001
Time	-0.763 [-1.088 – -0.438]	0.6149	< 0.001
Time squared	0.0367 [0.0216 – 0.0519]	0.0077	< 0.001

Changes in pre- and postoperative secondary outcomes

Cancer distress reduced significantly in time ($d=-0.36$, $p<0.001$) after 20 months. General physical health temporarily decreased at 6 months ($d=-0.41$, $p<0.001$), but returned towards baseline at 20 months (Table 3). No significant time effects were found for satisfaction with the partner relationship ($p=0.29$) and general mental health ($p=0.58$).

Table 3. Estimations and effect sizes at time points and covariate effects.

	Estimate	Difference with pre reconstruction		
		[95% CI]	p-value	effect size*
Body image				
<i>At mean of covariates</i>				
Pre reconstruction	3.04			
6 months	3.74	0.70 [0.55 – 0.84]	< 0.001	1.24
20 months	3.89	0.85 [0.70 – 1.00]	< 0.001	1.51
<i>Additional covariate effects</i>				
Partner relationship + 1 sd	0.15	0.15 [0.07 – 0.24]	0.001	0.27
Cancer distress + 1 sd	-0.19	-0.19 [-0.27 – -0.10]	< 0.001	-0.33
General mental health + 1 sd	0.11	0.11 [0.02 – 0.20]	0.019	0.19
Sexual relationship satisfaction				
<i>At mean of covariates</i>				
Pre reconstruction	8.48			
6 months	8.67	0.19 [0.04 – 0.33]	0.010	0.06
20 months	9.11	0.63 [0.15 – 1.10]	0.010	0.22
<i>Additional covariate effects</i>				
Hormonal therapy	-1.47	-1.47 [-2.61 – -0.33]	0.012	-0.51
Partner relationship satisfaction + 1 sd	1.54	1.54 [1.20 – 1.88]	<0.001	0.54
Cancer distress				
Pre reconstruction	20.4			
6 months	18.9	-1.46 [-2.13 – -0.78]	< 0.001	-0.11
20 months	15.5	-4.86 [-7.11 – -2.60]	< 0.001	-0.36
General physical health				
Pre reconstruction	53.3			
6 months	50.0	-3.56 [-4.68 – -1.83]	< 0.001	-0.41
20 months	52.7	-0.58 [-2.06 – 0.89]	0.43	-0.07

* Cohen's *d*

Discussion

This is the first prospective study showing that body image improves after delayed implant as well as DIEP flap BR and that it is not related to the type of BR.

The two patient groups did not significantly differ in most baseline variables. However, the fact that DIEP flap BR was only performed at the specialized centers, may impede the generalizability of the results, as the team of experts may be more aware of impact on body image and therefore may be more focused to reach the best outcomes after BR. Further, most bilateral breast reconstructions were performed using implants, which can be explained by logistic and financial limitations for bilateral DIEP flap BR in the Netherlands [41]. Evidently, DIEP flap BR patients had a significantly higher BMI as this type of surgery requires sufficient autologous tissue. Additionally, a high BMI may have been a contraindication for implant BR as this enhances the complication risk and a poor outcome [42]. In both BR groups the majority of the patients had received radiotherapy which may have damaged the skin, particularly in implant BR where the radiated skin envelope is used, in contrast to delayed DIEP flap BR in which healthy abdominal skin is used. Therefore, there might have been an interaction with the type of BR and radiotherapy, which was not investigated in this study.

A significant improvement in sexual satisfaction after both reconstruction types was detected, after correcting for relevant variables. Partner relationship satisfaction was positively related to sexual relationship satisfaction, highlighting the significant impact on the partner relationship if sexual function or satisfaction changes after breast cancer [43;44]. Having had hormonal therapy was related to a lower sexual relationship satisfaction score, as adjuvant therapy may induce premature menopause with negative sexual side effects including loss of libido and vaginal dryness [4;5;7;8;10-13;45]. BMI was not related to the sexual satisfaction score, but there might have been an interaction with the type of BR as well as women with DIEP flap BR had a higher BMI [46]. However, these were not the main research questions and therefore not investigated in the current study.

A large improvement in body image was observed which was significantly related to less cancer distress, higher satisfaction with the partner relationship and a better general mental health during the entire BR course. It has been previously demonstrated that changes in body image are related to psychological distress after mastectomy with or without reconstruction [47-49]. In accordance with previous findings, we found that mental health is positively related to body image as well [50].

To our knowledge, this is the first prospective study on body image and sexual satisfaction in patients with either delayed implant or DIEP flap BR [21]. We could not detect a statistically significant difference in body image and sexual satisfaction between implant and DIEP flap BR, whereas previous findings suggested a better outcome with autologous tissue, such as DIEP flap BR [20-23;51]. This can be explained by the retrospective designs and/or the inclusion of heterogeneous patient groups, such as patients with immediate as well as delayed BR. Timing of BR is important for body image and sexual satisfaction, as more positive outcomes have been found after autologous reconstructions if BR was delayed [19;20;22;52]. In addition, a relatively new approach of delayed-immediate BR, might reduce complication rates after radiotherapy, while preserving the skin and delaying breast reconstruction until radiotherapy is completed [53], which might positively influence body image as well. Nevertheless, no delayed-immediate BR was performed in our study population.

To focus on the difference between the types of BR, the current study concerned a homogenous group of patients all having delayed BR. It is notable that women with delayed BR may experience a greater increase in body image when compared to women with immediate BR. Women who opt for immediate BR will have a higher baseline body image score as they do not have the experience of mastectomy only because BR follows immediately during one operation. Women with delayed BR had to live for a while with a mutilated chest wall, resulting in a lower body image score before undergoing BR which provides more opportunity for improvement after surgery.

Ideally, each BR group in the present study should have included patients with immediate BR as well; however, in the Netherlands immediate DIEP flap BR after mastectomy for breast cancer is hardly performed due to shortness of reconstructive microsurgeons and other logistic limitations [41]. Another limitation is that patients could not be assigned randomly to a reconstruction type, as patients would subsequently have been withdrawn from complete information provision. A suggestion for future research is to further validate our BIS questionnaire and to use a breast reconstruction-specific questionnaire as well, such as the Breast-Q [54]. The NRV questionnaire assessed only the partner relationship and therefore excluded single women, future research should therefore focus on sexual satisfaction in single women as well. Finally, the sample size of the women with implant BR was small compared to the DIEP flap BR group as implant BR is generally provided immediately after mastectomy and therefore delayed implant BR patients were harder to include as this concerns a small patient group. Nevertheless, the number of women with a partner remained high in both groups regarding the NRV scores.

In conclusion, body image improved significantly after both implant and DIEP flap BR and a better general mental health, less cancer distress, and a better partner relationship satisfaction were related to a more positive body image before during the entire BR course. Sexual relationship satisfaction improved after both implant and DIEP flap BR, particularly if higher partner relationship satisfaction was reported. However, the psychosexual side effects of earlier hormonal therapy for breast cancer should be taken into account.

Clinical implications

It is important for clinicians to be aware of psychosocial aspects during the process of mastectomy followed by BR, next to satisfaction with aesthetic outcome. During postoperative follow-up consultations, the plastic surgeon and/or mamma-care nurse could specifically ask for the psychosocial impact of the breast cancer diagnosis and the psychosocial consequences of the cancer treatment, including the reconstructive procedure. Patients expressing that they experience problems should be referred to a medical psychologist who can teach the patient adaptive coping styles, help to regain intimacy and to process the event of having had cancer and the experience of adverse treatment side-effects on for example body image. This can lead to a better mental health which may positively affect body image, as well as physical health [55-57].

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Appendix 1. The body image scale

1. I was happy with my appearance when dressed
2. I felt very feminine
3. I was satisfied with my naked appearance
4. I had trouble looking at my naked self
5. I had trouble touching my breasts
6. I was satisfied with the appearance of my breasts
7. My breasts felt pleasantly
8. I felt sexually attractive
9. I felt comfortable enough to wear V-necked clothes
10. I felt comfortable enough to wear swimwear
11. I was embarrassed for my naked body
- 12 α . I felt comfortable when my partner touched my breasts
- 13 α . I had qualms about getting undressed in the presence of my partner

α : completed only by patients with a partner; item score 1-5: 1=totally disagree, 2=disagree, 3=neutral, 4=agree, 5=totally agree

CHAPTER 7 BODY IMAGE ISSUES AFTER BILATERAL PROPHYLACTIC MASTECTOMY WITH BREAST RECONSTRUCTION IN HEALTHY WOMEN AT RISK FOR HEREDITARY BREAST CANCER

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Abstract

Objective The outcome of bilateral prophylactic mastectomy with breast reconstruction (BPM-IBR) in healthy BRCA1/2 mutation carriers can be potentially burdensome for body image and the intimate relationship. Therefore, in the current analysis the impact on body image, sexual and partner relationship satisfaction was prospectively investigated in women opting for BPM-IBR as well as cancer distress and general quality of life.

Methods Healthy women undergoing BPM-IBR completed questionnaires preoperatively (T0, n=48), at 6 months (T1, n=44) and after finishing breast reconstruction (median 21 months, range 12-35) (T2, n=36). With multi-level regression analyses the course of outcome variables was investigated and a statistically significant change in body image and/or sexual and partner relationship satisfaction was predicted by baseline covariates.

Results Body image significantly decreased at T1. At T2 sexual relationship satisfaction and body image tended to be lower compared to baseline. The overall partner relationship satisfaction did not significantly change. At T2, 37% of the women reported that their breasts felt unpleasantly, 29% was not satisfied with their breast appearance and 21% felt embarrassed for their naked body. Most body image issues remained unchanged in 30% of the women. A negative body image was predicted by high preoperative cancer distress.

Conclusions BPM-IBR was associated with adverse impact on body image in a substantial subgroup, but satisfaction with the overall sexual and partner relationship did not significantly change in time. The psychosocial impact of BPM-IBR in unaffected women should not be underestimated. Psychological support should ideally be integrated both before and after BPM-IBR.

Introduction

Women with a BRCA1/2 mutation have a significantly increased cumulative lifetime risk for developing breast cancer (39-85%) as well as ovarian cancer (10-63%) [1-3]. One of the risk reducing strategies for developing breast cancer is bilateral prophylactic mastectomy usually including immediate breast reconstruction (BPM-IBR), which is associated with a risk reduction of more than 90% [4-6]. The decision for BPM-IBR among healthy BRCA mutation carriers in the Netherlands (33%) is one of the highest in the world, in line with data from the USA (36%) and the UK (40%) [7;8].

After BPM-IBR, women report reduced cancer distress and anxiety, at the cost however of potentially negative impact on body image and the intimate relationship [9-18]. Drawbacks of the previously reported studies are a retrospective design [10;12;15;19], and for the few available prospective studies performed in unaffected BRCA1/2 mutation carriers a limited follow-up period, maximally being up to one year postoperatively [9;14;16;20]. The single, prospective, long term follow-up study on the impact of prophylactic mastectomy with or without breast reconstruction included both *unaffected and affected* (history of breast and/or ovarian cancer) female BRCA mutation carriers (n=36), and showed ongoing problems with body image up to 6 to 9 years after PM/BR [11].

In the current study we focused on *unaffected* women, as the life event of having cancer may significantly disrupt quality of life, and more specifically the impact of BPM-IBR. We aimed to prospectively explore the course of 1) body image, and of satisfaction with the sexual and partner relationship, as well as of 2) cancer distress, and health related quality of life in women opting for BPM-IBR. The final assessment was planned after completion of the breast reconstruction process.

Methods

Patients

This study is part of a multicenter prospective follow-up study on the psychological impact of breast reconstruction, which was performed in both academic and regional hospitals in the Netherlands [21-23]. For the current analyses, participants were healthy (=unaffected) women at significantly increased risk of breast cancer due to a BRCA mutation or relevant family history who had opted for BPM-IBR. Exclusion criteria were suspicion of breast cancer in the planning towards BPM and a detection of breast cancer in the follow-up, and not being able to understand and speak the Dutch language sufficiently. Patients were approached between December 2007 and May 2010, and ethics approval was obtained from all participating hospitals⁵.

Seventy-three unaffected high-risk women scheduled for BPM-IBR were invited for the study by written information (academic hospitals: n=71, regional hospitals: n=2) and 50 women consented to participate (68%) (academic hospitals: n= 48, regional hospitals: n=2).

⁵ Leiden University Medical Center (LUMC), Erasmus University Medical Center Rotterdam (Erasmus MC), Daniel den Hoed Cancer Centre, Haga Teaching Hospital (Haga), Admiraal de Ruyter Hospital Goes.

Procedure

The invitation procedure has been described elsewhere [23]. Patients who returned informed consent, received the study questionnaires which they were requested to fill in preoperatively (T0). Similar questionnaires were sent at six months after BPM-IBR (T1), and after completing the BR process (T2). If BR was not completely finished (nipple reconstruction and/or nipple areola complex tattooing were planned but not yet performed) at the end of the follow-up period of the study, the final T2 questionnaire was still sent to measure the result at longer follow-up. The median follow-up time at T2 was 20.7 months, (mean = 21.7 months, range 12-35 months).

A maximum of two reminders were sent by letter if patients did not respond at T1 and/or T2, and patients were requested to provide a reason for non-compliance.

At least 75% of the respective questionnaires had to be filled in to calculate a scale score.

Measurements

Demographic information and clinical data were assessed with questionnaires and medical data were confirmed by checking medical records.

Primary outcome measuresBody image

We developed a study-specific body image scale (BIS) based on the Body Image/Sexuality questionnaire of Lodder et al. [24], who followed recommendations made by Cull [25] and Hopwood [26]. For conceptual reasons some items were adapted regarding the specific experience of going to the beach in bathing clothes, feeling comfortable in V-necked clothes, feeling comfortable when touched by the partner and feeling embarrassed when getting undressed in the partner's presence. The questionnaire consists of 31 items regarding the "past three months" which are scored on a five-point Likert scale. An explorative principal component analysis was performed in a large sample of women with therapeutic and/or prophylactic mastectomy with breast reconstruction, who had completed the questionnaire at multiple time points (n=442). Using the Scree-test criterion, we found a three-factor solution that accounted for 49.5% of the total variance. Items loading on one component exceeding 0.40 were considered to belong to a subscale. With a loading on two factors a difference of at least 0.09 was used.

The three-factor solution revealed three components of the 31 items: 1) a subscale measuring body image aspects (BIS-BIM) consisting of 13 items (see Table 4, explaining 19.8% of the total variance); 2) a subscale measuring the general importance of appearance (3 items, 7.6% of total variance, not shown); 3) a subscale measuring problems with intimacy (15 items, 22.1% of the total variance, not shown). For this study, only the first subscale, BIS-BIM, was used and the internal consistency of this subscale (13 items) proved to be good in the current study sample (Cronbach's $\alpha = 0.89$). The items were scored from 1-5 (totally disagree, disagree, neutral, agree, totally agree, respectively) and a mean scale score was calculated (1-5), where a higher score indicates a more positive body image. Two items

(12 and 13, see Table 4) were only completed by patients with a partner, however, for the single women a mean scale score was calculated as well as at least 75% (10 items) had to be completed.

To explore the occurrence of body image problems, items of the subscale BIS-BIM were recoded into three categories: 1 'disagree' (=1 and 2); 2 'neutral' (=3); 3 'agree' (=4 and 5) and relevant categories were reported in Table 4.

Satisfaction with the sexual relationship

Satisfaction with the *sexual relationship* was measured using the subscale 'sexuality' of the Dutch Relationship Questionnaire (Nederlandse Relatie Vragenlijst, NRV) including 11 items [27]. The NRV has shown good psychometric properties, and a total score on the subscale 'sexuality' below eight (range 0-12) indicates below average or low satisfaction with the sexual relationship and a bad sexual compatibility with the partner [27]. The NRV was completed only by patients having a partner.

Satisfaction with the overall partner relationship

Satisfaction with the overall partner relationship was investigated with the NRV as well (again only for patients with a partner). Normally, the total score of the NRV can be used to provide this satisfaction score. However, to correct for the impact of sexuality, the score of the 'sexuality' subscale was subtracted from the total score. Therefore, scores under 49 (range 0-68) indicate below average or low satisfaction with the partner relationship, excluding sexuality.

Secondary outcome measures

General physical and mental health were assessed with the Dutch version of the 36-item Short-Form Health Survey (SF-36) with respectively the Physical Component Summary (PCS) and the Mental Component Summary (MCS) of the SF-36 [28-30]. These scales concerned e.g. physical functioning, social functioning, vitality and bodily pain. In this norm based scoring method each scale has the same mean value (50) and standard deviation (10). Consequently, a scale score below 50 indicates that health status is below average [29].

Breast cancer specific distress was measured using the 15-items Impact of Event Scale (IES) [31;32]. The total IES score was used in this study with a range from 0 to 75. Reported reliability and validity of the IES are satisfactory [31;33]. The categorization of the IES score is not indicative for specific clinical diagnoses, but a cutoff score of 20 or higher can be used to indicate high symptom levels [33;34].

Statistical analyses

To investigate changes in time in the primary and secondary psychological outcomes, multi-level regression analyses (MLA) were performed, which can handle incomplete time-series data efficiently with a minimal loss of information. These analyses also compensate for different numbers of participants at each time point.

For the analyses of the time-course linear and quadratic time were included as covariates in the regression models. Effect sizes [35] were calculated by dividing the estimated differences by the estimated standard deviation at baseline. For the determination of body image course predictors a two-step procedure was applied. In the first step the number of potential covariates to be used in the MLA was reduced by calculating change scores between T0 and T1, and T0 and T2 and consequently by calculating their Spearman's Rho correlation coefficients with regard to age, having a partner, having children, type of BR, body mass index (BMI), having had prophylactic bilateral salpingo-oophorectomy (PBSO), the relationship with self-reported severe postoperative complications (=complications that lead to an unfinished result or removal of the reconstructed breast mound) and with the baseline psychological variables⁶. We applied a lenient p-value in order not to exclude covariates unduly, therefore the variables that correlated with the change scores ($p < 0.10$), were entered in the MLA. Continuous covariates were standardized to facilitate the interpretation of the estimates.

In a backward procedure all non-significant effects were removed from the model, until a parsimonious model was reached ($p\text{-out} > 0.10$). It was taken into account that interaction effects should be nested within the respective main effects [36]. The deviance statistic, that is the difference between the -2 residual log Likelihood fit measure of the final parsimonious model and the fit of the saturated model [37], was evaluated at a $p = 0.05$ level.

Finally, changes in proportions of the BIS-BIM-items (agree / disagree) in time were explored with the Cochran's Q-test in which the p-value represented a change in time (T0 / T1 / T2) in a related sample. Two-sided p-values $< .05$ were considered statistically significant and data were analyzed with the statistical package SPSS 17.0 (SPSS Inc., Chicago).

Results

Patient samples

Non-respondents ($n = 23$) and respondents ($n = 50$) did not significantly differ in age ($t_{(70)} = 0.77$, $p=0.44$). However, all non-respondents opted for implant BR compared to 19% of the respondents who chose DIEP flap BR (Fischer's Exact test, $p = 0.025$).

Two patients were excluded from further analyses as breast cancer was unexpectedly found in the mastectomy specimens. Seven women stopped participation and nine women did not respond at T1 and/or T2 regarding at least one of the questionnaires (Figure 1)⁷. Drop-out analysis was performed comparing these 16 patients with the 32 women with 100% response rate at all questionnaires during follow-up (Figure 1)⁸. Dropouts less often had a partner (69% vs 97%, Fisher's Exact test $p=0.012$), and reported a significantly lower sexual satisfaction level at baseline (mean=7.2, $sd=3.3$) compared to the active participants (mean=9.5, $sd=2.2$) ($t_{(39)}=2.38$, $p=0.022$). More dropouts had an unfinished breast reconstruction at the end of the follow-up study (69% vs 31%, Fisher's Exact test

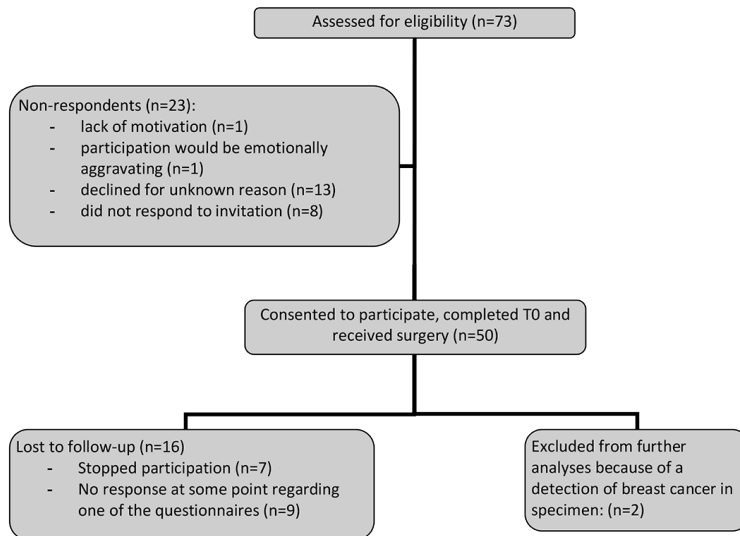
⁶ Correlation coefficients with body image change scores were calculated for the following baseline psychological variables: sexual and partner relationship satisfaction, cancer distress and general mental and physical health.

⁷ Dropout reasons: questionnaires were "too general" or "time consuming", having had complications, "there was no cancer distress as there was no cancer", and "not feeling psychologically stable"

⁸ Sexual and partner relationship satisfaction was only completed by women with a partner, therefore, N may be lower than 32 for these variables.

$p=0.001$). They did not differ significantly in the other medical, demographic and baseline psychological variables (data not shown).

Figure 1. Flow chart of patient inclusion



Demographic and clinical characteristics

Mean patient age of the study participants ($n=48$) was 37.1 years ($sd = 10.2$) yrs, range 21-65 yrs (Table 1). The majority had a partner ($n=42$) and children. Forty-four women were BRCA1/2 mutation carriers, one woman had an unclassified variant (UV), and three women opted for BPM-IBR based on the pedigree and risk estimation (belonging to non-BRCA1/2 mutation families)⁹. The minority (19%) underwent an autologous breast reconstruction with DIEP-flap (Table 1). Twenty-three percent had undergone PBSO at baseline and twelve women reported severe postoperative complications leading to an unfinished result or removal of the primary breast mound reconstruction.

Short term follow-up results from baseline (T0) to 6 months (T1) postoperatively

As shown in Table 2, a significantly less positive body image was detected at T1 compared to T0 ($p<0.001$). Satisfaction with the sexual as well as the overall partner relationship did not significantly change between T0 en T1, but sexual satisfaction tended to decrease ($p=0.07$). Cancer distress was above the cut-off score before surgery, and significantly decreased at T1 ($p<0.001$). General mental health at baseline was significantly improved at T1 ($p=0.02$). General physical health, at baseline significantly declined at T1 ($p<0.001$).

⁹ The four women without a BRCA1/2 mutation preferred PM over surveillance and after multidisciplinary consultation, they were allowed to have surgery.

Table 1. Baseline characteristics of 48 women opting for bilateral prophylactic mastectomy with immediate breast reconstruction (BPM-IBR)

Mean age in years at time of BPM-IBR (sd)	37.1 (10.2)
Having a partner	42 (87.5%)
Having children	31 (64.6%)
Education level	
primary education	10 (20.8%)
lower secondary education	20 (41.7%)
secondary and high education	18 (37.5%)
Breast cancer risk category	
BRCA1 carrier	33 (68.8%)
BRCA2 carrier	11 (22.9%)
Familial risk for breast cancer	4 (8.3%)
Type of breast reconstruction	
Implant	39 (81.3%)
DIEP-flap	9 (18.8%)
Mean BMI (sd)	25.1 (4.4)
Prophylactic bilateral salpingo-oophorectomy	11 (22.9%)
Severe complications*	12 (25.0%)

BMI: body mass index; DIEP: Deep Inferior Epigastric artery Perforator; SD: standard deviation; * self-reported severe complications that lead to an unfinished result or removal of the primary breast mound reconstruction

Longer term follow-up results from baseline (T0) to 21 months (T2) postoperatively

Body image and the sexual relationship satisfaction tended to decrease up to T2 (both $p=0.06$). The partner relationship satisfaction did not significantly change. Cancer distress significantly declined up to T2 ($p < 0.001$). For both general mental and physical health, the course did not significantly change from T0 to T2.

Predictors of a decreased body image after BPM-IBR

Correlation coefficients with the body image change scores ($p < 0.10$) revealed the following putative baseline covariates for body image (T0-T1; T0-T2): BMI ($r=0.28$, $p=0.07$, $n=44$ for T0-T1), cancer distress ($r=-.40$, $p=0.008$, $n=43$ for T0-T1; $r=-0.47$, $p=0.005$, $n=35$ for T0-T2) and general physical health ($r=-0.48$, $p=0.004$, $n=34$ for T0-T2). Therefore, BMI, baseline cancer distress and general physical health with their time interactions were entered into the saturated prediction model. Table 3 represents the final parsimonious model predicting the course of body image. It demonstrates that a preoperative cancer distress of 1 standard deviation higher than the average distress score leads to a decreased body image score of

Table 2. Psychosocial and psychosexual functioning before BPM-IBR, and 6 and 21 months postoperatively

	Parameter estimates			Time point estimates					
	Intercept	Time linear	Time quadratic	T1	T2	T0-T1		T0-T2	
						effect size	p	effect size	p
Body image (1-5) ^a	3.8****	-0.10****	0.0042****	3.3	3.5	-0.68	<0.001	-0.40	0.06
Sexual relationship satisfaction α (0-12) ^b	9.0****	-0.10*	0.31	8.5	8.0	-0.19	0.07	-0.35	0.06
Partner relationship satisfaction α (0-68) ^b	60****	-0.033	-0.0016	60	58	-0.03	0.79	-0.19	0.33
Cancer distress (0-75) ^c	23****	-2.4****	0.091****	12	13	-0.82	<0.001	-0.74	<0.001
General mental health ^d	48****	0.82**	-0.034**	51	50	0.38	0.02	0.23	0.19
General physical health ^d	55****	-1.5****	0.068****	48	53	-0.64	<0.001	-0.16	0.37

NOTE: the estimate for the intercept equals the estimate for T0. * p<0.10; ** p<0.05; *** p<0.001; **** p<0.001; BPM-IBR: bilateral prophylactic mastectomy and immediate breast reconstruction; T0: baseline assessment; T1: 6 months post-surgery; T2: 21 months post-surgery; ^aBody Image Scale; ^bDutch relationship questionnaire; ^cImpact of Event Scale; ^dShort Form – 36; α : completed only by patients with a partner; Higher scores indicate better outcomes, however for Cancer distress this is vice versa.

$6 \times -0.074 + 6 \times 6 \times 0.0033 = -0.33$ (Cohen's $d = -0.63$) at 6 months and a decrease of $21 \times -0.074 + 21 \times 21 \times 0.0033 = 0.10$ ($d = -.83$) at 21 months (Table 3). A high preoperative cancer distress score that leads to a more negative body image at long term follow-up applies to a quarter ($n=12$) of the women.

Furthermore, a higher preoperative general physical health predicted a better body image ($d=0.30$) and a lower BMI predicted a less positive body image ($d=-0.36$), in general, for women undergoing BPM-IBR.

Table 3. Predictors of the course of body image in women undergoing BPM-IBR

	Estimate [95% CI]	Std. Error	p-value
Intercept	3.76 [3.57 – 3.94]	0.09	<0.001
Time linear	-0.074 [-0.121 – -0.026]	0.024	0.003
Time quadratic	0.0033 [0.0011 – 0.0054]	0.0011	0.003
Preoperative cancer distress ^a	-0.118 [-0.304 – 0.067]	0.093	0.208
Time linear * preoperative cancer distress ^a	-0.076 [-0.124 – -0.028]	0.024	0.002
Time quadratic * preoperative cancer distress ^a	0.0025 [0.0004 – 0.0047]	0.0011	0.023
Preoperative general physical health ^b	0.172 [0.054 – 0.290]	0.059	0.005
BMI	-0.208 [-0.346 – -0.071]	0.068	0.004

BPM-IBR: bilateral prophylactic mastectomy and immediate breast reconstruction; ^aImpact of Event Scale; ^bSF-36: Short Form – 36; BMI: body mass index

Frequency of body image issues

Specific issues with body image are shown in Table 4 in which the items of the subscale BIS-BIM are presented. After BPM-IBR at T2, a significantly increased proportion ($p=0.001$) of women reported they were not happy with the appearance of their breasts (item 6, 29%) and the way their breasts felt (item 7, 37%), in particularly being the case at T1. At T1, a significant percentage did not feel feminine which was significantly higher compared to baseline and T2 ($p=0.02$).

For most items there was no significant change, substantial proportions remained having problems with their naked appearance (item 3, 20-30%), had trouble touching their breasts (item 5, 26-17%), felt sexually unattractive (item 8, 17-32%), were embarrassed for their naked body (item 11, 12-24%) and felt uncomfortable when the partner touched their breasts (item 12, 30-39%) before as well as after surgery.

Table 4. Number of women with body image problems before and after BPM-IBR regarding the “past three months” (BIS-BIM)

	T0		T1		T2		p-value*	
	N	%	n	%	n	%		
1. I was happy with my appearance when dressed [disagree]	36	2	5.6	3	8.3	4	11.1	0.69
2. I felt very feminine [disagree]	35	1	2.9	5	14.3	1	2.9	0.02
3. I was satisfied with my naked appearance [disagree]	35	7	20.0	12	34.3	11	31.4	0.20
4. I had trouble looking at my naked self [agree]	35	3	8.6	7	20.0	4	11.4	0.27
5. I had trouble touching my breasts [agree]	35	9	25.7	6	17.1	6	17.1	0.41
6. I was satisfied with the appearance of my breasts [disagree]	35	6	17.1	19	54.3	10	28.6	0.001
7. My breasts felt pleasantly [disagree]	35	7	20.0	21	60.0	13	37.1	0.001
8. I felt sexually attractive [disagree]	34	6	17.6	11	32.4	6	17.6	0.17
9. I felt comfortable enough to wear V-necked clothes [disagree]	35	3	8.6	5	14.3	7	20.0	0.30
10. I felt comfortable enough to wear swimwear [disagree]	35	3	8.6	8	22.8	4	11.4	0.05
11. I was embarrassed for my naked body [agree]	34	4	11.8	8	23.5	7	20.6	0.24
12 α . I felt comfortable when my partner touched my breasts [disagree]	23	8	34.8	9	39.1	7	30.4	0.65
13 α . I had qualms about getting undressed in the presence of my partner [agree]	30	1	3.3	6	20.0	5	16.7	0.07

BPM-IBR: bilateral prophylactic mastectomy with immediate breast reconstruction; BIS-BIM: body image subscale; T0: baseline assessment; T1: 6 months post-surgery; T2: 21 months post-surgery; * Cochran's Q test, overall difference in time. α : completed only by patients with a partner

Discussion

In women undergoing BPM-IBR mean body image scores decreased within the first 6 months after PM (T1), and it still tended to be lower after breast reconstruction (T2) compared to baseline. The mean scores of the partner relationship satisfaction did not significantly change in time, but the mean score of the sexual relationship satisfaction tended to decrease up to T2. When investigating specific body image issues on item level, we found that a substantial subgroup of the women reported problems after BPM-IBR, however, most issues already existed before surgery and did not change afterwards.

Comparing the number of women with body image issues in this study with corresponding samples of Lodder [24] and Den Heijer et al [11] the proportions of women with body image problems are similar. However, as there is a lack of body image data in a comparable age-matched healthy control group, we cannot tell how these proportions differ from the norm.

At 6 months, most women were in the middle of their breast reconstruction process. In particular women with implant breast reconstruction, who underwent a period of tissue expansion during the first months. At that point 55% was not satisfied with the appearance of their breasts. Although the majority had acceptable outcomes after BPM-IBR, the impact of BPM-IBR on body image and the intimate relationship should not be underestimated. There is a subgroup of patients at risk for developing a negative body image particularly during the breast reconstruction process (at T1) which should be taken into account during follow-up consults.

Our findings confirmed that prophylactic surgery results in a large reduction of cancer specific distress, which may be replaced by other problems, such as a decrease in physical health and a less positive body image during the BR process [9-18]. The total breast reconstruction course may cover a long period, up to 1.5 years, including expansion of tissue expanders, replacement with definite implants, additional aesthetic corrections and nipple reconstruction. After completion of breast reconstruction, physical health and body image may improve again.

It often happens that additional operations for complications or aesthetic reasons are needed after the primary breast mound reconstruction which is in accordance with our study findings [38-43]. Some women in this study experienced postoperative complications resulting in an unfinished result or poor breast reconstruction outcome. However, this was not related to a poorer body image, which can be possibly explained as a result of the small sample size. When calculating the change scores for the total observations (n=128) this variable indeed was negatively correlated with body image (data not shown).

It was an encouraging observation that the general mental health score improved significantly 6 months after BPM-IBR which might be explained by the initial relief from the reduction of the cancer risk due to the prophylactic mastectomy. Furthermore, the mean evaluation of the overall partner relationship remained stable and despite the tendency of a decline in the sexual relationship satisfaction, both mean NRV scores corresponded with normal norm scores [27]. Nevertheless, the trend towards a decline in sexual satisfaction, suggests that this finding could have been statistically significant in a larger sample.

A limitation of our study may be that no sexual *dysfunction* scale was included. A planned follow-up study shall provide more information about the issues in women with BPM-IBR regarding sexual dysfunction. We expect that sexual function might also be affected due to the consequences of (future) premenopausal PBSO, which is generally advised in BRCA1/2 mutation carriers [44;45]. This may result in adverse psychological, somatic and sexual consequences (e.g. vasomotor symptoms, vaginal dryness, decreased libido) [46-48]. Furthermore, future studies should include a validated breast reconstruction-specific questionnaire as well, such as the Breast-Q [49] for which norm data should be available as well to compare body image scores with a healthy age-matched norm group.

The study sample size was small; therefore MLA offered the best opportunity to analyze the data to correct for dropouts who had earlier reported worse scores on the psychological variables. An unfinished breast reconstruction procedure may have reinforced dropping out, as the dropout rate was significantly higher in this group. The full response rate on the body image questionnaire however, was high (75%), whereas it was lower for some of the other questionnaires (minimum response rate 67%). One of the reasons for this difference may be a lack of motivation to complete a whole battery of questionnaires. Some women had stated they did not want to complete the IES as they “did not have cancer and therefore did not have cancer distress”. Recruitment and participation of this patient group in long-term quantitative studies still is difficult and the small sample size is similar to comparable previous studies [11;13].

The main strength of this study is the prospective design, despite the small patient numbers. Our sample seems representative for healthy BRCA1/2 mutation carriers, including the finding that breast cancer was detected in the mastectomy specimens of two women [9;14;16;50;51]. Furthermore, the prediction model of body image provided medium to large effect sizes for the risk factor preoperative cancer distress, providing a good prediction for a negative body image after BPM-IBR [35]. We, therefore, recommend further exploring preoperative cancer distress in these patients and to pay more attention to those who are highly distressed to help them adapt better to their new body image after surgery. Nonetheless, a larger sample should be included in the future to confirm our findings and to support our inferences.

It is of great importance to inform patients *and* their partners about positive as well as negative consequences of BPM-IBR so they can form realistic expectations. This may help them to anticipate untoward side-effects after surgery [10;13;21;52-55]. It is preferable for all professionals involved to be aware of and enquire about psychosexual adjustment problems during follow-up visits. Psychosocial professionals should be sufficiently knowledgeable about onco-genetics. Psychological support should be offered after BPM-IBR in an integrated approach as long as the option for BPM-IBR is provided, as a substantial proportion of women face ongoing psychosocial issues [11;56].

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CHAPTER 8 SUMMARY, DISCUSSION AND IMPLICATIONS



1. Summary

1.1. Motivations for breast reconstruction

The motivations of women who opted for either implant or DIEP flap breast reconstruction (BR) after prophylactic or therapeutic mastectomy, were qualitatively explored by using interviews (Chapter 2). Before surgery, women were asked why they had opted for reconstruction and why they preferred a certain method. We observed that women generally decided in favour of reconstruction because they felt too young to live without breasts, wanted to avoid wearing an external prosthesis, and wished to feel feminine and self-confident which is in congruence with previous findings [1-3]. Motives to specifically opt for implant reconstruction were often primarily related to practical issues: preferring a short recovery period and a minimum number of scars in order to regain their daily life as soon as possible. Whilst they preferred a quick recovery, these patients may not have been aware of the fact that a complete BR course can take 21 months, which was the mean duration to the end of the BR in this study. Women who chose DIEP flap BR especially focused on regaining a breast that resembles their own lost breast as closely as possible. In addition, they had the idea that the complication risk of DIEP flap BR was lower compared to implant BR. Furthermore, they felt DIEP flap BR would offer long-term benefits and less secondary operations, whereas in fact the number of reoperations following complications after a mean follow-up period of 21 months was comparable in both groups (Chapter 4 and 5). Some patients preferred DIEP flap BR as it offered the additional advantage of an abdominoplasty. Nevertheless, it was apparent that next to personal motivations, clinical variables (such as therapeutic or prophylactic mastectomy, breast irradiation, availability of plastic surgeons with microsurgical expertise and long waiting lists) need to be taken into account when considering a certain type of BR, as these can have a marked influence in the decision making process as well.

1.2. Information seeking regarding breast reconstruction

As information provision concerning BR is not standardized in our country, being properly informed also depends on patients' information seeking behavior. Therefore, before surgery, we explored women's coping style and information seeking behavior (Chapter 3). We observed that women who had an active coping style and who were independent in their decision-making opted for DIEP flap BR. Women who were less well-informed and who depended more on their surgeon with regard to their decision opted for implant BR rather than DIEP flap BR. Before their operation, forty percent of the implant BR patients was not aware of the possibility of undergoing reconstruction with autologous tissue. To be well-informed about breast reconstructive surgery, an active coping style and independent information seeking was required, as not all women were sufficiently informed by their surgeon.

1.3. Complications after breast reconstruction

We found an overall complication rate of 40% after BR. These complications had a distinct impact on distress one month after BR (Chapter 4), when anxiety and cancer distress

significantly declined, but depression significantly increased. Forty percent of the patients with complications reported high levels of anxiety, depression and cancer-specific distress. Furthermore, we found a distinct difference between patients with implant and DIEP flap BR, in which the former were more anxious and had more cancer-specific distress, before their operation. This effect might have been affected by the timing of BR, as more women with implant BR underwent immediate reconstruction, meaning they had to undergo therapeutic mastectomy for breast cancer as well, ultimately resulting in higher cancer-distress.

After completion of the full BR course, anxiety decreased and depression was not significantly different from baseline levels. Both mean anxiety and depression levels were within the normal range (Chapter 5). Mean cancer distress was above the cut-off score before undergoing BR, but this significantly decreased, to normal levels, at the end of BR. In the long term, at the 21 months follow-up, complications and subsequent surgery generally did not lead to increased anxiety, depression or cancer distress, however, a permanent loss of BR (total removal of the reconstructed breast) did. The total loss of BR was significantly related to more depression and more cancer distress. Remarkably, women who had lost their BR already had higher cancer distress before undergoing BR. Younger patients had more anxiety and depression and their cancer distress was significantly higher at the end of BR. Furthermore, a longer period since mastectomy appeared to result in more anxiety and depression at the end of BR. These findings highlight that younger patients and women, who had the diagnosis of breast cancer a longer time ago, may still experience psychological adjustment problems even after the completion of the total BR course.

Before surgery, risk factors for developing higher psychological distress should be checked and women at risk for psychological distress should be carefully monitored after surgery with regard to their psychological wellbeing.

1.4. Body image and sexual satisfaction after breast reconstruction

The impact of either implant or DIEP flap BR on body image and sexual relationship satisfaction was prospectively investigated in women with delayed BR after a history of breast cancer (Chapter 6) and in healthy women with immediate BR after bilateral prophylactic mastectomy (Chapter 7). In the first group body image improved significantly after 20 months. A better body image was related to a better general mental health, less cancer distress and a higher partner relationship satisfaction. Sexual relationship satisfaction improved as well and a better partner relationship satisfaction was positively related to sexual relationship satisfaction; however, women who had hormonal therapy were less satisfied with their sexual relationship. No differences in body image and sexual relationship satisfaction were found with regard to the type of BR.

In healthy women, at risk for developing hereditary breast cancer, who underwent bilateral prophylactic mastectomy with immediate BR, body image significantly declined after 6 months and after 21 months body image still tended to be worse compared to the body image at baseline. The sexual relationship satisfaction tended to decline up to 21 months. However, the overall scores were within the normal ranges for body image and sexual satisfaction. Body image was positively related to general physical health, and negatively

to cancer distress. After completion of the total BR course, a significant subgroup reported that their breasts felt unpleasant, that they were not satisfied with their breast appearance and that they felt embarrassed about their naked bodies. Regardless of surgery, both before and after the operation one third indicated they felt uncomfortable when touched by their partner. These results indicate the psychosocial impact of bilateral prophylactic mastectomy with BR in healthy women should not be underestimated.

2. Discussion

Initially, the aim of this study was to compare the psychological impact of two types of BR: implant and DIEP flap BR in women who had breast cancer or who decided to have prophylactic surgery after being identified as carrier of a BRCA1/2 mutation. With a prospective multi-center design about 100 patients with implant and 100 patients with DIEP flap BR would be included. However, at the start of the study, many barriers were presented which made patient inclusion complicated. Each hospital appeared to have its favourite method of BR and showed a preference for offering BR either immediately or directly after mastectomy. Bilateral prophylactic mastectomies were generally performed in the academic hospitals. However, as patients were included in nine different hospitals, including academic centers as well as peripheral hospitals, patient inclusion for this study can be considered as representative for the Dutch patient population. Nevertheless, the reality is that the BR patient group is highly heterogeneous which would complicate statistical analyses and generalization of the study results.

Patient inclusion resulted in a study sample of 202 women who underwent BR. A total of 152 women had mastectomy as a treatment for breast cancer of whom 31 (20.4%) underwent contralateral prophylactic mastectomy as they were at high risk for developing breast cancer in the other breast as well. The remaining 50 women had bilateral prophylactic mastectomy to prevent the development of breast cancer as they had an increased risk for developing familial breast cancer. In total, about half of the women received implant BR and the other half had DIEP flap BR. However, due to practical (long waiting lists) as well as clinical (unavailability of autologous tissue) reasons bilateral prophylactic mastectomy was seldom followed by DIEP flap BR and therefore only concerned 10 out of 50 women in this sample. Consequently, the majority of these patients had implant BR. This impeded the statistical analyses from comparing the impact regarding the type of BR within the prophylactic group.

Next to the uneven distribution of the type of BR, the timing of BR was also unequally divided in the implant and DIEP flap group. Because DIEP flap BR requires an operative time of about four hours per breast, depending on the number of microsurgeons involved, bilateral prophylactic mastectomy followed by DIEP flap BR would take at least eight hours of surgery time, including closing of the abdominal donor-site. This requires the availability of an oncological surgeon, a plastic and reconstructive surgeon with microsurgical skills, a team of operating theatre personnel and enough theatre time on one day. However, the availability of microsurgeons with skills in perforator flap surgery is low. These practical limitations make it impossible to perform bilateral DIEP flap BR on a large scale, which is one

of the reasons why after bilateral (prophylactic) mastectomy the most commonly performed BR method is immediate implant BR [4;5].

Due to these difficulties a direct comparison between women with either implant or DIEP flap BR was strongly restricted. The difference between the types of BR was statistically measured by including the type of BR as a covariate in the longitudinal analyses. Nevertheless, we found that the type of BR was generally not related to most psychosocial outcomes after BR. As DIEP flap BR was generally performed as a delayed reconstruction method whereas implant BR was more commonly performed immediately after mastectomy, the role of the timing of BR may have been of great influence. Therefore, to specifically measure the impact of each type of BR, future studies should focus on an equal distribution of women with immediate and delayed BR for each BR type. It is to be expected that this type of patient inclusion would take many more years, to include a statistically acceptable sample size of women with DIEP flap BR after bilateral prophylactic mastectomy.

Ultimately, as each hospital has its own commonly performed type of BR, patient information provided before their operation is likely to have been biased. In Chapter 2 and 3 we found that not every patient was well informed regarding the possibility of implant BR or BR with autologous tissue. Autonomous patients and active information seekers chose the more sophisticated method of DIEP flap BR. In Chapter 5 it was demonstrated that women with DIEP flap BR had an overall higher satisfaction rate with the aesthetic end result compared to women with implant BR. This was expected as it is well-known that autonomous, aware patients are better-informed and have more realistic expectations, ultimately resulting in higher satisfaction with their decision afterwards [6-12]. On the other hand, cognitive dissonance [13] can lead to higher satisfaction as well: their intensive search for complete information and their physical efforts to undergo DIEP flap BR may have resulted in a positive attitude afterwards, reinforcing the notion that all the effort had been worth it.

Women with implant BR, the most commonly performed BR method, relied more heavily on their surgeon's advice regarding their decision for BR. In the interviews it appeared that some women were not prepared to go to a different hospital to get an autologous BR method, as for example a DIEP flap. As already mentioned, this technique requires microsurgical expertise and special education for the reconstructive surgeon and this expertise is only available in specialized centers. This availability consequently resulted in long patient waiting lists for DIEP flap BR, which in turn was a further restriction for some patients. However, Damen et al. demonstrated that aesthetics and the complication risk were of greater importance than the long waiting lists in the decision for BR [14]. Nevertheless, the results of this study demonstrate that standardized information provision regarding BR options, and availability of the different techniques per hospital, is needed for patients to enable them to make the best decision.

As mentioned, autologous BR requires highly skilled and qualified surgeons and the operation takes a long time, resulting in much larger costs compared with implant BRs. Health care costs are increasing rapidly in the western world and efforts are being made to reduce these costs. Expensive operations, such as autologous BR should be given due credit

for their ability to improve the quality of life compared to, for example, implant BR and more research on the (cost-) effectiveness of autologous BR, using QALYs (Quality Adjusted Life Years) is needed [5].

The impact of the overall complication rate after BR (40%) was investigated in Chapter 4 and 5. A major limitation of these studies was that the questionnaires were not sent directly after a complication occurred and consequent additional surgery was conducted, therefore a causal relationship could not be identified. It was demonstrated that women with a failed BR had worse psychosocial outcomes. However, the clinical experience is that currently these women are rarely followed up by most hospitals, except for the period until all surgical wounds have healed. Once it becomes clear that the plastic surgeon cannot offer a new BR during this period, women often leave the outpatient clinic without a future planned follow-up consultation or the offer of psychological counseling.

In Chapters 6 and 7 the impact of BR on body image was described. A study-specific questionnaire was used which was adapted from the previous studies of our research line [15;16]. Some questions were revised and other questions were added designed specifically to address the impact of BR. We collected a total number of observations on the body image questionnaire of $n=442$, which provided more statistical power compared to the previous studies ($n=14$ and $n=19$) [15;16]. A new three-factor solution revealed different outcomes than Lodder et al. [15] had reported, and therefore study results could not be easily compared to previous study findings [15-17].

We decided not to include a control group of women undergoing mastectomy without BR as it had been previously demonstrated that generally psychosocial outcomes do not differ between women with BR and patients without BR [18-32]. In addition, our data on the standardized and validated questionnaires could be compared with normative data to place the data in context. Motivations whether to choose for BR or not were also previously explored, however to compare motivations for either implant BR, DIEP flap BR or no BR, we interviewed a small sample of women who had not undergone BR.

Undergoing the process of having breast cancer and/or dealing with an increased familial breast cancer risk requires many resources from the patient as well as from the partner. The intimate relationship can be negatively influenced after mastectomy [33-50]. We measured the course of overall sexual and partner relationship satisfaction during the process of BR using the validated NRV questionnaire (Dutch Relationship Questionnaire) [51]. As this instrument was designed only for couples or persons with a partner, single women were excluded. Because mastectomy and BR will undoubtedly impact single women's intimate relationships, future studies need to assess sexuality outcomes in this group well.

Psychological distress and its predictors were evaluated by means of both global distress measures (anxiety and depression) as well as a breast cancer-specific questionnaire, as an indicator for psychological adjustment. These instruments have been frequently used in similar studies world-wide and their psychometric values have been well established. However, these measures may not have been sensitive enough to capture the specific concerns and personal issues of our study population as has been recently demonstrated by Vos et al [52].

2.1. Implications for future studies

This prospective multi-center study regarding two types of BR represents the heterogeneous patient population undergoing BR for breast cancer. The majority of patients had good psychosocial outcomes after both BRs. However, subgroups of patients reported worse outcomes, such as women who had experienced a loss of the reconstructed breast(s). Remarkably, we noticed that psychosocial issues after having BR are hardly discussed and explored during routine follow-up consultations by medical professionals. Future studies should focus on the care and communication with psychologically vulnerable patients.

Future studies aiming to evaluate the psychological outcomes after therapeutic and prophylactic mastectomy, and/or being at risk for hereditary breast cancer should also include outcome measures specific to the field of mastectomy and hereditary breast cancer. In view of the potential impact of mastectomy and BR, the Breast-Q would be a worthwhile addition [53]. For the specific impact hereditary breast cancer has on self-concept, we support the idea of Espen et al. [54] that it would be particularly interesting to use the BRCA Self-Concept Scale as an outcome measure for this patient group. In addition, we recommend to include validated questionnaires regarding intimate or relational aspects for single persons as well.

Furthermore, more prospective studies with a follow-up period beyond 18 months to assess the psychosocial impact of BR are needed [55;56]. Most prospective studies include a maximum follow-up of 12 months [27;57-61], therefore a longer follow-up period after BR is recommended for future research to explore longer term outcomes after BR as well. Also, the specific issues and help needs of patients with regard to intimacy, including single women as well as partnered patients together with their partners, should be further scientifically explored.

Overall, we have to bear in mind that quantitative research reduces the individual impact to mean group scores, whereas in clinical practice we should focus on the individual and inter-relational impact. This means the individual impact of BR on body image, sexual and partner relationship satisfaction, anxiety, depressive feelings and cancer worries. Qualitative studies are therefore a useful addition to the quantitative data. Our range of research on BR will be expanded in the near future and will include qualitative interviews as well with patients and partners.

2.2. Recommendations for the clinical practice

Based on the study findings, participants' comments during the follow-up and patient reactions at the patient day, organized at the end of the study, our recommendations for the clinical practice are the following:

- include the partner from the beginning in the medical consultations
- stimulate each patient to be assertive; encourage her to explicitly ask for the information she is missing during the process of mastectomy with BR
- before the operation, show the patient pictures of good and moderate BR results (organize show and tell sessions)

- before the operation, inform the patient about the complication risks and possible psychological adjustment problems, particularly regarding the period shortly after surgery
- involve a case-manager (e.g. the mamma-care nurse) in the mastectomy and BR process from before surgery to the end of BR
- routinely provide, before the operation, a psychological consultation for the patients who are about to undergo prophylactic mastectomy, in order to inform and prepare these often young women on possible (adverse) changes in body image and intimacy
- after the operation, offer a consult with a psychologist to the women who underwent prophylactic mastectomy
- the impact of severe complications on general wellbeing should be addressed by the surgeon or mamma-care nurse
- at any time, the mamma-care nurse and other specialists involved should refer patients with persisting psychological adjustment problems to a psychologist.
- emphasize that psychological help remains available during the whole recovery process
- Inform patients about patient organizations and websites (BVN, Pink Ribbon; www.borstkanker.nl; www.BRCA.nl; www.pinkribbon.nl)

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SAMENVATTING

1. Borstkanker

1.1. Sporadische borstkanker

In Nederland is borstkanker het meest voorkomende type kanker bij vrouwen en is de kans 1 op 8 om dit in haar leven te krijgen. Ieder jaar worden er meer dan 13000 nieuwe gevallen geconstateerd, waarvan de meeste vrouwen ouder dan 50 jaar oud zijn [1]. Daarom worden vrouwen in Nederland tussen de 50 en 75 jaar sinds 1989 uitgenodigd om deel te nemen in het nationale bevolkingsonderzoek, om iedere twee jaar de borsten te screenen op borstkanker, om zo nodig vroegtijdige behandeling te starten en het aantal sterfgevallen te verminderen [2-4]. Er bestaan diverse behandelingen voor borstkanker, zoals chirurgie, chemotherapie, bestraling en hormoontherapie. Ondanks het toepassen van borst besparende operaties, met of zonder nabehandeling, is het in 46% van de gevallen nog steeds nodig om een mastectomie te ondergaan [5].

1.2. Erfelijke borstkanker

Ongeveer 5% tot 10% van alle borstkankergevallen worden veroorzaakt door een genetische afwijking [6]. Vrouwen uit families met een BRCA1/2 mutatie hebben een significant verhoogd risico om in hun leven borstkanker te ontwikkelen (39-85%) als ook eierstokkanker (10-63%) [7-9]. Deze vrouwen worden een apart screeningsprogramma voor de borsten aangeboden, waaronder een jaarlijkse MRI-scan, een mammografie en klinisch borstonderzoek. Vrouwen met een verhoogd risico op borstkanker gebaseerd op de familiegeschiedenis, wordt ook een apart screeningsprogramma aanbevolen, zoals geadviseerd in de Nederlandse Borstkanker Richtlijnen (2011). Omdat een screeningsprogramma vroegtijdig borstkanker kan opsporen, maar het ontstaan er van niet kan voorkomen, kan preventieve mastectomie ook besproken worden met deze hoog-risico vrouwen [10-12].

2. Mastectomie en borstreconstructie

2.1. Therapeutische mastectomie met borstreconstructie

Een mastectomie kan een grote impact hebben op het lichaamsbeeld en zelfbeeld van de vrouw, zoals zich abnormaal of depressieve voelen, een gevoel van incompleetheid, en rouwgevoelens omtrent het verlies van de borst [13-17]. Borstreconstructie (BR) kan patiënttevredenheid en lichaamsbeeld significant verbeteren na mastectomie [18-23]. Echter, andere psychologische uitkomsten lijken niet significant te verschillen tussen vrouwen met en zonder BR na mastectomie [24-28]. Recent is onderzocht dat BR geassocieerd wordt met een verlaagde kans op sterfte na borstkanker, vergeleken met vrouwen die geen BR ondergingen, maar alleen een mastectomie, maar dit wordt waarschijnlijk verklaard door sociaal economische factoren zoals toegang en mogelijkheden van de gezondheidszorg, dan door oncologische factoren [29;30].

Het aantal patiënten dat een BR krijgt varieert van 10% tot 40% en neemt toe. Echter, er is een grote etnische en geografische variatie, waarbij bijvoorbeeld niet blanke vrouwen en patiënten wonend in afgelegen gebieden, minder snel BR ondergaan [31]. In Nederland

ondergaat naar schatting 20% van de vrouwen BR na therapeutische mastectomie, de meerderheid ondergaat dus geen BR [32].

2.2. Preventieve mastectomie met borstreconstructie

Preventieve mastectomie (PM) wordt gezien als een effectieve methode om het borstkankerrisico met meer dan 90% te reduceren in vrouwen met een verhoogd risico op het ontwikkelen van borstkanker [10-12;33;34]. De combinatie van het kankerrisico, de angst voor kanker en toenemende mogelijkheden om de borsten te reconstrueren na mastectomie, heeft de optie voor PM populairder gemaakt. Meer dan tien jaar geleden koos 55% van de Nederlandse, gezonde, hoog-risico vrouwen voor bilaterale PM [34], maar recentelijk is dit percentage gedaald naar 33% [35]. Redenen om geen bilaterale PM te ondergaan kunnen gerelateerd zijn aan mogelijk negatieve effecten op lichaamsbeeld en seksualiteit [36-46]. Daarnaast zijn er tegenwoordig betere screeningstechnieken beschikbaar die borstkanker in een eerder stadium kunnen opsporen [47-52] en het is aannemelijk dat deze verbeterde diagnostische technieken dokters en patiënten ervan weerhouden om te kiezen voor bilaterale PM. Desondanks, is de keuze voor bilaterale PM nog steeds hoog in Nederland, vergeleken met het internationale percentage van 18% [35;53]. Alleen in Amerika (36%) en Engeland (40%) ligt dit percentage hoger. Het percentage is het laagst in Polen (3%), Israël (4%) en Noorwegen (5%). Ten opzichte van contralaterale PM bij hoog-risico vrouwen die eerder borstkanker hadden in de andere borst, is het percentage in Nederland ook hoog (53%), vergeleken met internationaal (27%) [54;55]. Deze grote variatie kan ook te maken hebben met culturele verschillen, waarin zowel dokters als patiënten een rol kunnen spelen.

Tegenwoordig wordt BRCA1/2 mutatie dragsters ook geadviseerd om de eileiders en eierstokken preventief te laten verwijderen (PBSO) om het risico op eierstokkanker te reduceren [56;57]. BRCA1 mutatie dragsters wordt geadviseerd om PBSO te ondergaan tussen de 35 en 40 jaar oud, terwijl voor BRCA2 mutatie dragsters geadviseerd wordt om dit tussen de 40 en 45 jaar oud te doen (Nederlandse Richtlijnen voor Erfelijke Tumoren 2010). Deze risicoreducerende operaties kunnen een aanzienlijk effect hebben op het psychosociale welzijn. PBSO kan de menopauze opwekken, wat kan leiden tot negatieve gevolgen op psychologisch, lichamelijk en seksueel gebied, waaronder een verminderde libido, opvliegers en vaginale droogheid [58-60].

2.3. Type borstreconstructie

In het algemeen zijn er drie soorten BR te onderscheiden: met siliconen implantaten, lichaamseigen weefsel of een combinatie van beide. Een BR met siliconen implantaten wordt het meest uitgevoerd [61;62], meestal voorafgegaan door plaatsing van een weefselexpander achter de borstspier. Hiermee worden de borstspier en borsthuid geleidelijk opgerekt [63], zodat de expander na een paar maanden vervangen kan worden door een definitief implantaat.

Er zijn verschillende BR technieken mogelijk met lichaamseigen weefsel, waarbij vaak huid, vet en soms ook spierweefsel wordt gebruikt van een donorplaats elders in het lichaam, zoals de Latissimus Dorsi (LD) lap (de rugspiermethode) [64]. De Transverse

Rectus Abdominis Myocutaneous (TRAM) lap bestaat uit huid, vet en spierweefsel van de onderbuik dat gesteeld of vrij gevasculariseerd wordt verplaatst naar de borstwand [65]. Andere autologe BR technieken zijn de Gluteal Artery Perforator (GAP) lap en de Transverse Myocutaneous Gracilis (TMG) lap, die bestaan uit huid en vet van de bil en huid, vet en spier uit het mediale dijgebied [66;67]. Op dit moment is de meest populaire BR methode met lichaamseigen weefsel de Deep Inferior Epigastric Artery Perforator (DIEP) lap, bestaande uit huid en vet van de buik. Bij deze methode worden de buikspieren intact gelaten, waarmee de kans op abdominale spierzwakte of een breuk afneemt [68]. Echter, dit vereist microchirurgische expertise van de reconstructief chirurg en deze deskundigheid is alleen beschikbaar in gespecialiseerde centra, wat resulteert in lange patiëntwachlijsten en hogere kosten. In het algemeen wordt er een hogere tevredenheid en een beter lichaamsbeeld na autologe BR gerapporteerd, vergeleken met implantaat BR, maar meer prospectieve studies zijn nodig om dit te bevestigen [37;69-74].

2.4. Tijdstip van borstreconstructie

BR kan worden uitgevoerd hetzij direct, op hetzelfde moment met mastectomie of uitgesteld; maanden of jaren na de mastectomie. Er is een gerandomiseerde gecontroleerde trial (RCT) uitgevoerd waarin de specifieke gevolgen van directe versus uitgestelde BR onderzocht werd, waarbij drie maanden postoperatief directe BR werd geassocieerd met betere psychosociale uitkomsten in vergelijking met uitgestelde of geen BR [20]. Het random toewijzen aan een type of tijdstip van BR wordt echter over het algemeen als onethisch gezien met betrekking tot het achterhouden van informatie en het niet naleven van patiënt voorkeuren, waardoor er geen andere RCT op dit gebied verricht is sinds 1983. Cross-sectionele en cohortstudies hebben aangetoond dat het esthetisch resultaat over het algemeen beter is na directe BR, omdat de huid envelop en af en toe de tepel gespaard kunnen worden [69;75;76]. Vrouwen die een mastectomie met directe BR ondergaan, hebben mogelijk ook voor de operatie een beter zelfbeeld, meer zelfrespect en voelen zich seksueel aantrekkelijker dan vrouwen die al een mastectomie hebben en op het punt staan om een uitgestelde BR te ondergaan [77]. Het tijdstip van BR is van groot belang hier, omdat vrouwen met een uitgestelde BR een periode hebben geleefd met slechts één of geen borsten en daarom een grotere kans hebben om verbetering te ervaren; hun lichaamsbeeld en seksuele bevrediging, bevinden zich wellicht op het laagste punt vóór de BR. Na uitgestelde BR is het complicatie risico lager gebleken vergeleken met directe BR [75]. In combinatie met het *type* BR, zijn er meer positieve resultaten over lichaamsbeeld en seksuele bevrediging gevonden na een *uitgestelde* autologe BR [37;69;71;73]. Tot slot, heeft het tijdstip van BR geen invloed op de incidentie van een recidiverende borstkanker en vrouwen die een directe BR hebben, ervaren geen vertraging in adjuvante behandeling ten opzichte van vrouwen die geen BR ondergaan [29;78-80].

3. Psychologische aspecten van borstreconstructie

Dit proefschrift focust op de impact van twee verschillende types BR na mastectomie: de meest uitgevoerde BR methode met siliconenimplantaten en de meest geavanceerde BR

methode die gebruik maakt van lichaamseigen weefsel van de buik: de DIEP-lap BR. Bij aanvang van deze studie was er nog maar weinig bekend over de psychosociale uitkomsten van de DIEP-lap BR [71;74;81-83]. Daarom werd met de huidige studie onderzocht wat de mogelijke voor- en nadelen waren van dit type BR, vergeleken met implantaat BR. De effecten van demografische en andere klinische variabelen op de psychosociale uitkomsten werd ook onderzocht. Hieronder volgt een korte samenvatting van de onderzoeksresultaten van de studie die in dit proefschrift wordt beschreven.

3.1. Motieven voor borstreconstructie

De motivatie van vrouwen om te kiezen voor implantaat of DIEP-lap BR vanwege profylactische of therapeutische mastectomie, is kwalitatief onderzocht met behulp van interviews (hoofdstuk 2). Voor de operatie, werden vrouwen gevraagd waarom ze hadden gekozen voor BR en waarom ze specifiek kozen voor een bepaalde BR-methode. In overeenstemming met eerdere bevindingen kozen patiënten voor BR omdat ze zich te jong voelden om door het leven te gaan zonder borsten, wilden het dragen van een externe prothese voorkomen, en wensten zich vrouwelijker en zelfbewuster te voelen. Motieven om specifiek te kiezen voor implantaat BR, hadden voornamelijk betrekking tot praktische kwesties: een korte herstelperiode en een minimum aantal littekens hadden de voorkeur, zij wilden hun dagelijkse leven zo spoedig mogelijk hervatten. Desondanks bleek de totale BR procedure achteraf circa 21 maanden te duren. Vrouwen die specifiek voor DIEP-lap BR kozen waren vooral gericht op het terugwinnen van een borst die zoveel mogelijk op hun eigen verloren borst zou lijken. Deze patiënten vonden tevens dat het complicatie risico van dit type BR lager was vergeleken met implantaat BR. Bovendien vonden zij dat DIEP-lap BR op de lange termijn voordelen zou bieden, zoals minder secundaire operaties, terwijl het aantal secundaire operaties na complicaties, na een gemiddelde follow-up tijd van 21 maanden, vergelijkbaar was in beide groepen (hoofdstuk 4 en 5). Sommige patiënten hadden ook de voorkeur voor DIEP-lap BR omdat het een extra voordeel van een buikwandcorrectie bood. Niettemin was het duidelijk dat naast persoonlijke motivaties met klinische variabelen (zoals therapeutische of profylactische mastectomie, bestraling, beschikbaarheid van plastische chirurgen met microchirurgische expertise en lange wachtlijsten) rekening gehouden moet worden bij het overwegen van een bepaald type BR, omdat deze ook een belangrijke rol spelen in de besluitvorming.

3.2. Informatie-zoekend gedrag over borstreconstructie

Omdat informatievoorziening over BR niet gestandaardiseerd is in ons land, is het van belang dat patiënten zelf ook op zoek gaan naar informatie, willen zij naar behoren worden ingelicht. Daarom is voor de operatie het informatiezoekende gedrag van deze patiënten onderzocht (hoofdstuk 3). We hebben vastgesteld dat vrouwen met een actieve coping stijl en die zich onafhankelijk opstelden van hun plastische chirurg, eerder kozen voor een DIEP-lap BR. Vrouwen die minder goed geïnformeerd waren en die zich afhankelijker van hun chirurg opstelden met betrekking tot hun besluit, kozen eerder voor een BR met implantaten. Voor de BR operatie, was 40% van de patiënten zich niet bewust van de mogelijkheid van BR met

lichaamseigen weefsel. Om goed geïnformeerd te zijn over borstreconstructieve chirurgie, was een actieve coping stijl en autonomie nodig, omdat niet alle vrouwen voldoende op de hoogte waren via de informatie van hun chirurg.

3.3. Complicaties na borstreconstructie

We vonden een complicatie-ratio van 40% na BR. Deze complicaties had een duidelijke invloed op distress één maand na BR (hoofdstuk 4), waarbij angst en kankergerelateerde distress aanzienlijk daalden, maar depressie aanzienlijk steeg. Veertig procent van de patiënten met complicaties rapporteerde hoge niveaus van angst, depressie en kanker-specifieke zorgen. Bovendien vonden we een duidelijk verschil tussen patiënten met implantaat en DIEP-lap BR, waarin de eerste angstiger waren en meer kanker-specifieke zorgen rapporteerden. Dit effect zou echter te maken kunnen hebben met het tijdstip van BR omdat meer vrouwen met implantaat BR direct na de mastectomie de reconstructie ontvingen, wat betekent dat zij mogelijk ook nog aanvullende behandelingen voor de borstkanker moesten ondergaan, resulterend in hogere kankerspecifieke distress.

Na voltooiing van de volledige BR procedure, waren angst en depressie niet meer significant verschillend van de niveaus voor de operatie. Bovendien waren de niveaus van angst en depressie binnen het normale bereik (hoofdstuk 5). Kankerspecifieke distress was voor de BR operatie echter boven het normale bereik, maar dit daalde sterk direct na de BR tot aan het einde van BR. Op de lange termijn, 21 maanden na BR, leidden complicaties en hierop volgende secundaire operaties over het algemeen niet tot meer angst, depressie, of kankerspecifieke distress, echter, dit was niet het geval indien er sprake was van een permanent verlies van BR (totale verwijdering van de gereconstrueerde borst). Het totale verlies van BR was aanzienlijk gerelateerd aan meer depressie en meer kankerspecifieke distress. Opmerkelijk was, dat vrouwen die hun BR hadden verloren, al hogere kankerspecifieke distress hadden voordat zij BR ondergingen. Jongere patiënten hadden ook meer angst en depressie en hun kankerspecifieke distress was aanzienlijk hoger aan het einde van BR, dan bij oudere patiënten. Bovendien, bleek een langere periode tussen de mastectomie en de BR te leiden tot meer angst en depressie aan het einde van BR. Deze bevindingen benadrukken dat jongere patiënten en vrouwen, die de borstkankerdiagnose een langere tijd geleden ontvingen, nog steeds psychologische aanpassingsproblemen kunnen ondervinden, zelfs na de voltooiing van de totale BR procedure. Voor de operatie, is het al van belang dat risicofactoren voor het ontwikkelen van psychologische distress worden gecontroleerd en vrouwen met een verhoogd risico voor distress moeten zorgvuldig worden opgevolgd na de operatie met betrekking tot het psychologische welzijn, naast de follow-up van het fysieke herstel.

3.4. Lichaamsbeeld en seksuele tevredenheid na borstreconstructie

De impact van implantaat of DIEP-lap BR op lichaamsbeeld en de seksuele relatie tevredenheid werd onderzocht bij vrouwen met een uitgestelde BR, na een geschiedenis van borstkanker (hoofdstuk 6) en bij vrouwen met een directe BR na bilaterale profylactische mastectomie (hoofdstuk 7). In de eerste groep, was lichaamsbeeld 20 maanden na BR aanzienlijk

verbeterd. Een beter lichaamsbeeld is gerelateerd aan een betere algemene mentale gezondheid, minder kankerspecifieke distress en een hogere partner relatie tevredenheid. Tevredenheid met de seksuele relatie verbeterde ook en was positief gerelateerd aan de algehele tevredenheid met de partnerrelatie; echter, vrouwen die hormonale therapie hadden ondergaan waren minder tevreden met de seksuele relatie. Dit kan mogelijk verklaard worden door de negatieve bijwerkingen van hormonale therapie op het seksuele functioneren.

Gezonde vrouwen met een verhoogde kans op het ontwikkelen van erfelijke borstkanker, die kozen voor een bilaterale profylactische mastectomie met directe BR, hadden 6 maanden na de operatie een aanzienlijk lager lichaamsbeeld dat ook na 21 maanden nog niet terug was op het niveau van voor de operatie (hoofdstuk 7). De tevredenheid van de seksuele relatie verminderde tot 21 maanden na de operatie. Lichaamsbeeld was positief gerelateerd aan algemene fysieke gezondheid, en negatief gecorreleerd aan kankerspecifieke distress. Na voltooiing van de totale procedure van BR, rapporteerden een substantiële groep dat hun borsten onaangenaam aanvoelden, ze waren niet tevreden met hun borsten en ze schaamden zich voor hun naakte lichaam. Zowel vóór als na de operatie gaf circa een derde van de patiënten aan dat ze zich ongemakkelijk voelden wanneer ze werden aangeraakt door de partner. Deze resultaten wijzen erop dat de psychosociale gevolgen van bilaterale profylactische mastectomie met BR bij gezonde vrouwen niet mag worden onderschat.

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Jessica Premdee Gopie was born on May 5th, 1985 in Leidschendam, the Netherlands. She graduated from secondary school in 2003 (VWO, Alfrink College te Zoetermeer) and started directly with her study Psychology at the University of Leiden. She obtained her Bachelor's degree in 2006 and her Master's degree in Clinical Psychology in October 2007 after conducting research at the Department of Psychosomatic Gynaecology and Sexology in the Leiden University Medical Center (LUMC). Her Master's thesis focused on the psychological characteristics of women with chronic pelvic pain.

In August 2007, she started with her PhD study regarding the psychological impact of breast reconstruction after mastectomy, as described in this thesis, at the Department of Clinical Genetics in the LUMC, in collaboration with other departments from the LUMC and the Erasmus Medical Center Rotterdam. She obtained funding from the Pink Ribbon Foundation in the end of 2011 to expand her research line as a Post-doc, focusing on the longer term psychological impact of prophylactic and therapeutic surgery for breast cancer, in particular, regarding the impact on body image, sexuality and the partner relationship. In addition, she received funding from the Pink Ribbon Foundation to organize a patient day (September 2012) and in collaboration with Pink Ribbon she plans to set up a psychological group intervention for women who underwent prophylactic mastectomy and their partners (2013).

She also works as a clinical psychologist in the onco-genetics, providing psychological support to patients and their partners, for which she obtained her degree in the Psychosocial Oncology in June 2012 from the RINO Groep Academy. She is also involved in other research projects regarding the impact of surveillance and prophylactic surgery of other hereditary tumors and is involved in the working group of Familial Tumours of the Dutch Society for Psychosocial Oncology, in the Dutch Guidelines for Hereditary Ovarian Cancer and in the Dutch Guidelines for Breast Reconstruction. In September 2013 she will start with the training for professional health-care psychologist (Opleiding tot Gezondheidszorg Psycholoog) in the LUMC.

CURRICULUM VITAE

Jessica Premdee Gopie is geboren op 5 mei 1985 in Leidschendam. Zij heeft in 2003 haar VWO diploma behaald aan het Alfrink College te Zoetermeer en startte aansluitend haar studie Psychologie aan de Universiteit Leiden. Zij heeft haar Bachelor's diploma in 2006 gehaald en haar Master's diploma in de Klinische Psychologie in oktober 2007, nadat zij onderzoek deed op de afdeling Psychosomatische Gynaecologie en Seksuologie van het Leids Universitair Medisch Centrum (LUMC). Haar masterthese had betrekking op de psychologische eigenschappen van vrouwen met medisch onverklaarde, chronische buikpijnklachten.

In augustus 2007 startte zij met haar promotieonderzoek over de psychologische impact van borstreconstructie na mastectomie, zoals beschreven in dit proefschrift, op de afdeling Klinische Genetica van het LUMC, in samenwerking met andere afdelingen van het LUMC en het Erasmus Medisch Centrum Rotterdam. Zij heeft eind 2011 een subsidie ontvangen van Stichting Pink Ribbon om haar onderzoeklijn verder uit te breiden als postdoc, waarmee zij de langere termijn psychologische impact van profylactische en therapeutische chirurgie vanwege borstkanker verder onderzoekt, in het bijzonder met betrekking tot lichaamsbeeld, seksualiteit en de partnerrelatie. Daarnaast heeft zij ook een subsidie van Stichting Pink Ribbon ontvangen om een patiëntendag te organiseren (september 2012) en zijn er gezamenlijk met de stichting plannen om een psychosociale groepsinterventie te ontwikkelen voor vrouwen die profylactische mastectomie hebben ondergaan en hun partners (2013).

Ook verricht zij klinisch werk als psycholoog binnen de onco-genetica, waarin zij patiënten en partners ondersteuning biedt omtrent de psychosociale gevolgen van (erfelijke) kanker. In juni 2012 heeft zij haar diploma in de Psychosociale Oncologie behaald bij de RINO Groep. Verder is zij betrokken bij andere onderzoeksprojecten naar de impact van screening en profylactische chirurgie bij verschillende erfelijke tumoren en is zij lid van de werkgroep Familiaire Tumoren van de Nederlandse Vereniging van Psychosociale Oncologie en betrokken bij de totstandkoming van de Nederlandse Richtlijnen voor Erfelijk Ovarium Carcinoom en de Nederlandse Richtlijnen voor Borstreconstructie. In september 2013 zal zij starten met de Opleiding tot Gezondheidszorgpsycholoog in het LUMC.

PUBLICATIONS

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