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Which Breast is the Best?

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Which Breast is the Best?

Patient Reported Quality of Life, Satisfaction,
and Outcomes, after Autologous versus Alloplastic
Breast Reconstruction

Yassir Eltahir

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Patient Reported Quality of Life, Satisfaction, and Outcomes, after Autologous versus Alloplastic Breast Reconstruction

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Which Breast is the Best?

Patient Reported Quality of Life, Satisfaction,
and Outcomes, after Autologous versus
Alloplastic Breast Reconstruction

Proefschrift

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CHAPTER 1

General Introduction

GENERAL INTRODUCTION

Introduction outline

This thesis “Which Breast is the Best” aims to contribute to our understanding of which Breast reconstruction (BR) technique (alloplastic or autologous), results in the highest quality of life (QoL) and satisfaction. The first section of this introduction will cover breast cancer and its treatment briefly, the second section will discuss the history and summary of the BR techniques. Thirdly, the topic of quality of life assessment and breast-Q will be described. As well as the assessment of aesthetical outcome will be covered, using the Strasser score. Finally the aim of this thesis and its outline will be given.

Breast Cancer

Breast cancer (BC) is the most common cancer in females worldwide and a leading cause of cancer-related mortality¹. In the Netherlands it is also the most common cancer amongst females (26%), about 17,000 women are diagnosed with breast cancer per year². Approximately 1 in 7 women in the Netherlands suffer from breast cancer at some stage in their lifetime and each year around 3,000 women die as a consequence of it². The treatment of breast cancer has greatly improved in the past 125 years. Initially the only treatment option was surgical, in which case radical mastectomies were performed, removing all breast tissue, overlying skin and the pectoralis major and minor muscles were also removed³. Halsted described this radical mastectomy procedure for treating breast cancer in 1894³. This radical mastectomy was a mutilating surgery. Nowadays, breast cancer is treated multidisciplinary. The latest diagnostic methods of radiology, pathology and gene expression are applied to determine the specific type of breast cancer in order to select the best evidence based treatment protocol. This may include neoadjuvant and/or adjuvant chemotherapy, radiotherapy, hormone and/or immunotherapy⁴. Surgical treatment consists of skin sparing mastectomy with or without nipple sparing, and with or without sentinel lymph node excision or axillary block dissection⁵. Mastectomy is performed as a therapeutic, as well as a prophylactic procedure, to prevent breast cancer. Prophylactic mastectomy is offered to women with genetic increased risk of developing breast cancer and reduces this risk by 90-95%⁶.

Breast conserving therapy (BCT) was introduced as an alternative option for mastectomy in an attempt to preserve part of the breast and prevent amputation. Radiotherapy is an integral part of BCT and aims to reduce the risk of local cancer recurrence⁷. Radiotherapy maybe given with or without boost. Despite these advances in treatment of breast cancer, mastectomy remains an important tool for surgical treatment⁷.

As mentioned, prophylactic Mastectomy (PM) can be offered to women with documented breast cancer related gene mutations⁸. The *BRCA1/2* genes mutations, among others, increase the risk of developing breast cancer, the cumulative breast cancer risk to age 80 years is 72% for *BRCA1* and 69% for *BRCA2* carriers⁹.

Gene mutation carriers may also choose for intensive breast cancer screening, which is performed with an annual MRI-based breast exam, which begins at the age of 25¹⁰. In *BRCA 1* carries, screening MRI will be combined with mammography every second year starting at the age of 40¹⁰. In *BRCA 2* carries, annual screening mammography is started age 30 years old¹⁰ from age 60 years both groups of *BRCA 1* and *BRCA 2* carriers are screened with annual mammography only¹⁰. Finally, from age 75 on, screening is no longer needed¹⁰. However, some of the *BRCA* carrier patients choose risk-reducing mastectomy over breast screening in order to avoid the anxiety of frequent tests, false positives results, and the high likelihood of a cancer diagnosis followed by the morbidity of treatment¹¹. Different factors may be associated with woman's decision for PM instead of intensive BC screening to reduce the risk associated with *BRCA1* or *BRCA2*^{11,12}. Identifying those factors and the baseline characteristics of women with gene mutation, may provide information about the reason for their decision and give valuable insight that can be discussed with these women.

Having to undergo a mastectomy undoubtedly compounds a traumatic, life-changing event in women diagnosed with breast cancer¹³. Beside psychological changes¹⁴ and the concerns about their health, women are also apprehensive about their appearance following this disfiguring operation¹⁵. This disconsolate perception may impact their social, personal and sexual relationships¹⁶. For these women, breast reconstruction (BR) may be considered as a possible solution¹⁷.

BREAST RECONSTRUCTION

There are two surgical methods to reconstruct a missing breast. In autologous reconstruction, a woman's own tissue is used and in alloplastic implants are used.

Autologous Breast Reconstruction (BR) involves the transfer of skin, fat and sometimes muscle from different area of the body to the mastectomy site. Historically Verneuil probably described one of the first cases of autologous BR¹⁸. He defined the use of part of the contralateral breast as a pedicled means to BR in 1887¹⁸. Czerny performed the first free autologous procedure in 1895¹⁹, when he attempted breast augmentation by transplanting a lipoma into a breast¹⁹.

The modern era of autologous BR already started in 1906 with the application of the latissimus dorsi myocutaneous flap (LD) by Tansini¹⁹. Autologous BR techniques underwent many changes with the evolving anatomic knowledge and improvement of surgical techniques. In 1979, Holmstrom¹⁹ was the first to use the normally discarded tissue following an abdominoplasty as a free flap in breast reconstruction. Shortly thereafter, an important alternative was introduced when Hartrampf et al described the pedicled transverse rectus abdominis myocutaneous flap (TRAM) in 1982¹⁹. This was followed by another important advancement when Allen and Blondeel described the inferior epigastric perforator flap (DIEP) as a refinement (with less donor site morbidity) to the TRAM flap^{19,20}. Plastic surgeons continue

this tradition of searching for refinements and alternatives in techniques, and have since designed flaps such as the lumbar flap²¹, laparoscopically assisted DIEP Flap Harvesting²² or lipofilling for partial or total BR²³. For now the DIEP flap is, when possible, the best option for autologous BR.

Gersuny attempted the first alloplastic BR in 1889, using paraffin injections¹⁸. Notwithstanding this, the alloplastic BR era really started in 1961, when Cronin and Gerow introduced the first silicone implants¹⁸. Twenty years later, Radovan described the concept of tissue expansion and published his results with tissue expansion for breast reconstruction in 1982²⁴. The quality and design of implants have undergone great advancements in the past four decades, which so far have resulted in four generations of implants with different textures, shapes and fillings²⁵. In the 1990s due to fear of capsular contracture, textured implants²⁶ were popularized at the expense of smooth implants²⁷, as textured implants demonstrated a lesser propensity for capsular contraction than their smooth counterparts²⁸. Nowadays, we again see that the pendulum is swinging back in the other direction with an increase in the use of smooth implants due to the association of textured surface with Breast Implant Associated-Anaplastic Large Cell Lymphoma (BIA-ALCL)²⁹.

Mortality and morbidity were for long the primary outcomes used to determine the success of breast cancer surgery. However, in the last decades breast surgeons and reconstructive surgeons have primarily aimed at decreasing the complication risks and are now gradually moving their attention towards improving the patients' Quality-of-life (QoL). To measure the patient's reported QoL and outcomes, various questionnaires were developed to allow the collection of data on quality of life and satisfaction from the patients. A patient reported outcome measurement (PROM) is far more than a mechanism for gathering opinion, it is designed to measure a specific concept in a standardized way³⁰. Thus, it provides a means of quantifying qualitative information³⁰. In case of BR, these PROM instruments help to understand what works best for women undergoing BR regarding their QoL and satisfaction. Improvement of QoL and satisfaction are these days regarded as of utmost importance in care provided by plastic surgeons³¹.

This paragraph gives a brief summary of the different instruments developed to collect patients reported data. Most of the questionnaires were generic, such as EuroQoL group (EQ-5D)³². It is one of the most frequently used generic instruments³² which can be applied in various diseases. It is a preference-based instrument and measures respondents' health status using a utility index³². But this is not a condition-specific measurement. Another generic questionnaire is the Short Form 36, which has 36 items to assess the QoL. Although it is widely used, it has not been validated for Breast cancer nor BR³³. The functional assessment of cancer therapy-breast (FACT-B) is a validated QoL patient reported outcomes tool. But it has not been validated for BR either³³. The EORTC-Q30/Q23, are a general and a breast cancer specific QoL instruments, usually used together³³. Despite having been validated for breast cancer, both were not certified for BR³³. The QLQ-BRR26, is a BR specific instrument. It is still undergoing phase 3 development, and inten-

tion is to use it alongside EORTC QLQ-C30/Q23³³.

The Breast-Q was designed to gauge the impact on quality of life (QoL) and satisfaction of mastectomy and breast reconstruction patients³⁴. It is a specific QoL-measuring instrument for breast surgery patients, which was developed following the international patient reported outcomes measure guidelines³⁴. Patient interviews, focus groups, expert panels, and a literature review were used to develop a conceptual framework and a list of questionnaire items³⁴. Breast surgery patients' input was incorporated in each step of the development³⁴. Furthermore, the Breast-Q was developed using qualitative and quantitative psychometric methods, and it exceeds international criteria for rigorous measurement³⁴. It is currently one of the few case specific instruments of patient reported outcome measures in reconstructive breast surgery that meets the international standards in terms of development and validation³⁵.

The Breast-Q consists of 3 modules: Augmentation Module, Reduction/Mastopexy Module and Breast Cancer module³⁶. The breast cancer module is subdivided into a Mastectomy Module, Reconstruction Module, Breast Reconstruction Expectations Module and Breast Conserving Therapy (BCT) Module³⁶. Each module is comprised of two domains: the QoL and patient satisfaction³⁶. Each module is divided into multiple scales. The scales are psychosocial, physical, sexual well-being and satisfaction with breasts, satisfaction with outcome and satisfaction with care³⁰. Each module has preoperative and postoperative scales. Each scale can be independently used³⁴. The outcomes of the scales are transformed into scores from 0 to 100. Thus, each scale displays a score from 0 (very dissatisfied) to 100 (very satisfied)³⁴. The Breast-Q has been translated in many language. We translated it into Dutch and the latter translation was validated in accordance with the agreement with the MAPI Trust (<http://www.mapi-trust.org/>) and ultimately approved by Dr. Pusic, the Principal developer of the Breast-Q. The first version of the Breast-Q was published in 2009³⁷.

A good aesthetic outcome is another important endpoint of breast reconstruction. Standardized photographs are used for subjective assessment. Several photographs measurement scales have been developed, such as the BRA and panel scoring³⁸, the breast retraction assessment³⁹, the BRA and PBRA⁴⁰, 4 measures of distances between fiducial points⁴¹ and the ratios of distances between fiducial points⁴². Although they all have limited utility for full aesthetic assessment, they have been used to assess postoperative outcome in women with breast cancer. The photograph measurement scales rely on anatomical landmarks such as the inframammary fold or nipple and they involve only a single photograph for each patient⁴³. Furthermore, 3D digital imaging to evaluate the volume, surface area, shape, size, contour and asymmetry has been employed^{44,45,46}. 3D imaging has great potential for pre and postoperative analysis of breasts. However, it does have limitations for women with large and/or ptotic breasts and maybe influenced by position changes⁴³.

The gold standard scoring system for breast aesthetics is still lacking. There is no well-established, validated, or reproducible scoring systems for doctors or panels to use when rating aesthetic outcomes after breast reconstruction.

However, the Strasser Grading System was applied in aesthetic plastic surgery to provide an objective and reproducible grading of the aesthetic outcomes⁴⁷. This system includes five subscales that grade malposition, distortion, asymmetry, contour deformity, and scar on 16-point scales⁴⁷. When the result is perfect or no flaws are seen, the score is 0; 1 is the score in case of any noticeable flaw, 5 for an obvious flaw and 15 for an obvious and deforming flaw⁴³. All points are added to get a total score ranging from 0 to 75, with an overall score of 0 indicating a perfect result, 1–4 a good result, 5–14 a mediocre result, and 15 or more a poor result⁴³.

Aim

The main aim of this thesis is to determine which BR technique, alloplastic or autologous results in the highest QoL and satisfaction in women after successful autologous or alloplastic BR. To achieve this aim the following studies have been designed and executed:

- The baseline characteristics of *BRCA* 1/2 carriers who opt for risk reducing mastectomy (RRM) early on, following the disclosure of identified DNA test results.
- The QoL outcomes and satisfaction of women after BR were investigated and compared to those who underwent mastectomy only, using the Breast-Q and other health-related QoL measures.
- The literature was reviewed and meta-analyzed to assess the patients' perspective on alloplastic versus autologous post mastectomy BR as measured by the Breast-Q. To evaluate which BR technique would give the best improvement in individual QoL and achieve satisfaction as measured with the Breast-Q.
- The satisfaction and QoL of women post successful BR were evaluated with the Breast-Q to investigate whether autologous or alloplastic BR may result in higher QoL.
- The relationship between the breast reconstruction method and the patient's satisfaction was studied to evaluate aesthetic outcome among women who underwent breast reconstruction after mastectomy.

OUTLINE OF THE THESIS

1

Chapter 1: Provides a general introduction and outline of this thesis. **Chapter 2:** Risk-reducing mastectomy in *BRCA1/2* mutation carriers: factors influencing uptake and timing. The baseline characteristics of gene mutation *BRCA1/2* carriers was investigated, to evaluate which features affect women's early decision for risk reducing mastectomy (RRM). The patient characteristics data were prospectively collected. Univariate and multivariate survival analyses were preformed to calculate the percentage of women undergoing RRM over time. **Chapter 3:** Quality of Life outcomes between patients undergoing mastectomy only and mastectomy followed by breast reconstruction using the Patient-reported Breast-Q and other Health-related QoL (RAND-36) measures. Demographic information, patients' anxiety, depression and concerns about recurrences were measured by using standardized questionnaires. This is a cross-sectional study of patients treated between 2006 and 2010. Linear regression modelling and multiple regression analyses were performed. **Chapter 4:** Outcomes of quality of life for women undergoing autologous versus alloplastic breast reconstruction post-mastectomy. A systemic review and meta-analysis. A review was designed to study papers which compared autologous BR versus alloplastic BR and used the Breast-Q in their study. The research in **Chapter 5** was designed to answer the question: 'Which Breast Is Best?' Following successful Autologous or Alloplastic Breast Reconstruction Patient-Reported Quality-of-Life Outcomes and the satisfaction was investigated. The breast-Q instrument and standardized questionnaires on depression, recurrence concerns and anxiety were used. The PROM data were studied to identify which BR technique leads to satisfaction. Descriptive statistics were applied in this cross-sectional study to describe the baseline characteristics. Multiple regression analyses were preformed to investigate the PROM data. **Chapter 6:** Satisfaction with cosmetic outcomes of breast reconstruction: investigation into correlation between the patients' Breast-Q outcomes and the judgment of the panels. An independent panel used the Strasser score to evaluate the cosmetic results based on postoperative photographs. The relationship between the panel score, the Breast-Q scores and the BR technique were investigated. Mann-Whitney U tests were used in this cross-sectional study to compare the Breast-Q and Strasser scores for each type of BR. **Chapter 7:** provides the general discussion and future perspectives.

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CHAPTER 2

Risk-Reducing Mastectomy in *BRCA1/2* Mutation Carriers: Factors influencing Uptake and Timing

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ABSTRACT

Introduction

Strategies in case of high risk of breast cancer in *BRCA1/2* mutation carriers are either intensive breast cancer screening or risk-reducing mastectomy (RRM). Both options have a high physical and psychosexual impact. The aim of this study is to investigate who chooses when to undergo RRM.

Methods

BRCA1/2 mutation carriers have been prospectively registered at the family cancer clinic between 1994 and 2011. Analyses were performed to assess the relation between characteristics of the *BRCA1/2* mutation carriers and an earlier decision for RRM

Results

A cumulative percentage of 35.6% of all women chose to undergo RRM within the first five years after disclosure of DNA test results. Women needed less time to choose for RRM measured from the first visit, if they were younger than 50 years of age (hazard ratio (HR)=2.67, 95% confidence interval (CI)=1.30-5.48) or had a mother who had had breast cancer (HR=1.51 95% CI=1.04-2.18). Also, women needed less time to choose for RRM in case of a previous breast cancer (HR=2.25, 95% CI=1.55-3.27). After a previous unilateral therapeutic mastectomy as a treatment for breast cancer, women needed less time to choose for RRM of the contralateral breast (HR=2.69, 95% CI=1.29-5.62) compared to women who had had breast-conserving therapy.

Conclusion

BRCA1/2 mutation carriers aged under 50, having a mother with breast cancer, who had previous unilateral breast cancer and previous unilateral therapeutic mastectomy chose more often and earlier for RRM.

INTRODUCTION

Women with a *BRCA1* or *BRCA2* mutation have a significantly higher lifetime risk of developing breast cancer and are diagnosed at a younger age compared to the general population¹⁻⁴. The lifetime risk at the age of 70 years for breast cancer was found to be 57-65% for *BRCA1* and 45-49% for *BRCA2* mutation carriers^{1,2}.

BRCA1/2 mutation carriers have to make major decisions regarding the medical management of their increased breast cancer risk. To reduce the risk of death due to breast cancer, women can choose for risk-reducing mastectomy (RRM) or they can opt for intensive breast cancer screening aiming at early detection^{5,6}. When performed at a young age, before the cancer risk is rising, RRM is associated with an actual breast cancer risk reduction of 90-95%⁷. However, RRM has been associated with a negative impact on body image⁸.

A review including 43 published articles identified three main types of factors that influence high-risk women's decisions about risk-reducing strategies: a) medical and physical factors, b) psychological factors and c) social context factors. How these factors operate in women's lives over time remained unknown⁹.

The purpose of this study was to identify baseline characteristics of *BRCA1/2* carriers that opt for RRM early on following the disclosure of DNA test results. Identifying which characteristics influence the (early) decision for RRM can indicate important topics to be discussed during counselling.

METHODS

Patients

Women with an increased risk of carrying a *BRCA1/2* mutation are referred to the clinical genetic department of the University Medical Centre Groningen for genetic risk assessment. Those that have a high cancer risk are followed-up at the Family Cancer Clinic (FCC) with a multidisciplinary team including clinical geneticists, surgical oncologists, gynecological oncologists, plastic surgeons, social workers, nurse practitioners and a psychologist¹⁰. When visiting the FCC women were asked to give informed consent for entering their data into a prospectively maintained password protected FCC database. Protection of the patients' identity was guaranteed by assigning study-specific, unique patient numbers. According to Dutch law no further Institutional Review Board approval was needed for this study.

Data collection

Women were included in this study if they were proven *BRCA1/2* mutation carriers and had visited the FCC between April 1994 and November 2011 at least once. As according to Dutch guidelines RRM should preferably be offered to women from the age of 25 years, only women ≥ 25 years of age were included in this study.

We considered the disclosure date of the *BRCA1/2* mutation to the patient as the first moment of contact and the last visit was considered to be the most recent visit to the FCC or the most recent visit to the FCC before RRM. The date of first contact and the date of the last visit were extracted from the (digital) patient files and used to calculate follow up times. For this study, characteristics concerning the patient as well as her family were collected. Patient characteristics concerned: age, mutation status and medical history. The medical history concerned previous breast and/or ovarian cancer, related treatment and risk reducing strategies. Patient characteristics were retrieved from the prospectively maintained FCC database. Family characteristics concerned: number and age of children and breast and/or ovarian cancer within the family, both at the time of the first visit to the FCC. Family characteristics were derived from non-electronic clinical genetics records.

Statistical analysis

Survival analysis was chosen to demonstrate the course of decision making over time, since this method adjusts for variable follow-up time. Univariate and multivariate survival analyses were performed over the total group of women (women opting for RMM as well as opting for intensive breast cancer screening), in order to calculate the cumulative percentage of women undergoing RRM over time, hazard ratios (HR) and the 95% confidence intervals (CI) of the baseline characteristics where the timing of the decision to undergo RRM was considered dependent.

The disclosure date of the *BRCA1/2* mutation to the patient was considered as the first moment of contact. The last moment of contact was considered to be the most recent visit or the most recent visit to the FCC before RRM. All tests were performed in SPSS Statistics 20 package and all p-values were two-tailed and considered significant if $p \leq 0.05$.

RESULTS

Description of the population

From April 1994 until November 2011, 508 *BRCA1/2* carriers ≥ 25 years of age had visited the FCC (figure 1). Women were excluded if a RRM was performed before the first visit to the FCC ($n=10$), if they had had bilateral breast cancer or disseminated disease ($n=38$) and if their clinical files were not available ($n=21$) or were incomplete ($n=30$). Two women were excluded due to mild mental retardation and inability to make their own decisions ($n=2$). The number of women included in the analysis was 407. Patient characteristics are given in Table 1.

Figure 1. Population flowchart

All *BRCA1/2* mutation carriers ≥ 25 years old entered in the FCC database at November 2011 ((n=508) from April 1994 – November 2011)

Determinants of the timing of the decision to undergo RRM

Within the first five years after disclosure of DNA test results a cumulative percentage 35.6% women chose to undergo RRM (Table 1). In table 2 it is shown that in the multivariate survival analysis, women younger than 50 years needed less time after counselling to decide for RRM than women > 50 years of age (HR=2.87 95% CI=1.40-5.92, $p=0.0042$). Furthermore, women who had a mother with breast cancer needed less time to decide for RRM (HR=1.51 95% CI=1.04-2.18, $p=0.031$). Women previously diagnosed with unilateral breast cancer decided earlier for RRM of the contralateral breast than women without a breast cancer history (HR=2.54, 95% CI=1.74-3.70, $p<0.001$). Of the women with previous breast cancer, those who underwent therapeutic mastectomy as a therapy for a unilateral breast cancer needed less time to choose for RRM of the contralateral breast (HR=2.69, 95% CI=1.29-5.62, $p=0.008$) compared to women who had breast conserving therapy (table 3).

Table 1. Characteristics of the study population at the time of DNA test disclosure and the uptake of RRM within 5 years of follow-up (N = 407).

Patient characteristic		Frequencies at the time of DNA disclosure	Cumulative uptake of RRM after 5 years	Cumulative deferral of RRM after 5 years
Overall		N.A.	35.6%	64.4%
Age	<50	335/407 (82.3%)	38.4%	61.6%
	≥50	72/407 (17.7%)	20.7%	79.3%
Mutation status	<i>BRCA1</i>	255/407 (62.7%)	40.9%	59.1%
	<i>BRCA2</i>	152/407 (37.3%)	25.8%	74.2%
Children	No	97/402 (24.1%)	27.9%	72.1%
	Yes	305/402 (75.9%)	38.1%	61.9%
Age youngest child	<18	219/301 (72.8%)	43.5%	56.5%
	≥18	82/301 (27.2%)	25.1%	74.9%
Mother with BC	No	246/398 (61.8%)	30.6%	69.4%
	Yes	152/398 (38.2%)	44.2%	55.8%
Sister with BC	No	300/399 (75.2%)	33.4%	66.6%
	Yes	99/399 (24.8%)	41.2%	58.8%
Mother with OC	No	316/402 (78.6%)	38.7%	61.3%
	Yes	86/402 (21.4%)	24.6%	75.4%
Sister with OC	No	357/395 (90.4%)	36.5%	63.5%
	Yes	38/395 (9.6%)	28.7%	71.3%
BC ^a in history	No	291/407 (71.5%)	26.3%	73.7%
	Yes	116/407 (28.5%)	61.3%	38.7%
Number of BC ^a	1	107/116 (92.2%)	61.8%	38.2%
	>1	9/116 (7.8%)	100.0%	0.0%
Therapy of first BC ^a	Lumpectomy	45/112 (40.2%)	31.4%	68.6%
	Mastectomy ^b	67/112 (59.8%)	74.5%	25.5%
OC in history	No	391/407 (96.1%)	36.2%	63.8%
	Yes	16/407 (3.9%)	19.6%	80.4%

N.A., not applicable; BC, breast cancer; OC, ovarian cancer; RRSO, risk reducing salpingo-oophorectomy; RRM, risk reducing mastectomy. **a** This concerns unilateral breast cancer, RRM of the contralateral breast remained medical management option. **b** Unilateral therapeutic mastectomy.

Table 2. Analysis of the determinants of the timing of the decision for RRM (uni- and multivariate survival analysis)

Patient characteristic		Univariate HR (95% CI) p-value	Multivariate HR (95% CI) p-value
Age	<50	2.67 (1.30-5.48) 0.007	2.87 (1.40-5.92) 0.004
	≥50	1	1
Mutation status			
	BRCA1	1.76 (1.16-2.67) 0.008	
	BRCA2	1	
Has children			
	No	1	
	Yes	1.26 (0.81-1.97) 0.30	
Age youngest child			
	<18	2.18 (1.21-3.92) 0.01	
	≥18	1	
Mother with BC			
	No	1	1
	Yes	1.52 (1.05-2.20) 0.03	1.51 (1.04-2.18) 0.03
Sister with BC			
	No	1	
	Yes	1.35 (0.90-2.03) 0.15	
Mother with OC			
	No	1	
	Yes	0.66 (0.41-1.07) 0.09	
Sister with OC			
	No	1	
	Yes	0.74 (0.36-1.52) 0.42	
BC* in history			
	No	1	1
	Yes	2.25 (1.55-3.27) <0.001	2.54 (1.74-3.70) <0.001
OC in history			
	No	1.15 (0.42-3.12) 0.79	
	Yes	1	
RRSO			
	No	1	
	Yes	1.20 (0.79-1.84) 0.39	

BC: breast cancer, OC: ovarian cancer, RRSO: risk reducing salpingo-oophorectomy.

* This concerns unilateral breast cancer, RRM of the contralateral breast remained medical management option. Result significant when $p < 0.05$.

Table 3. Analysis of the determinants of the timing of the decision for RRM in the subgroup of *BRCA1/2* carriers with previous breast cancer (N=116).*

Patient characteristic		Univariate HR (95% CI) p-value
Age	<50	3.20 (1.15-8.92) 0.03
	≥50	1
Mutation Status	<i>BRCA1</i>	1.57 (0.76-3.25) 0.23
	<i>BRCA2</i>	1
Has children	No	1.23 (0.64-2.38) 0.54
	Yes	1
Age youngest child	<18	4.00 (1.55-10.33) 0.004
	≥18	1
Mother with BC	No	1
	Yes	1.62 (0.90-2.91) 0.11
Sister with BC	No	1
	Yes	1.04 (0.56-1.92) 0.90
Mother with OC	No	1
	Yes	0.60 (0.25-1.41) 0.24
Sister with OC	No	1
	Yes	0.34 (0.08-1.42) 0.14
Number of BC**	1	2.72 (0.37-19.89) 0.32
	>1	1
Therapy of first BC*	Lumpectomy	1
	Mastectomy***	2.69 (1.29-5.62) 0.008
OC in history	No	1
	Yes	0.85 (0.20-3.50) 0.82
RRSO	No	1
	Yes	1.84 (0.95-3.58) 0.072

BC: breast cancer, OC: ovarian cancer, RRSO: risk reducing salpingo-oophorectomy

* As in the multivariate results only therapy of first BC contributed, only univariate results are presented

** This concerns unilateral breast cancer, RRM of the contralateral breast remained medical management option.

*** Unilateral therapeutic mastectomy

Result significant when $p < 0.05$.

DISCUSSION

Women needed less time to choose for RRM if they were younger than 50 years of age (HR=2.87 95% CI=1.40-5.92), had a mother with breast cancer (HR=1.51 95% CI=1.04-2.18), had previous unilateral breast cancer (HR=2.54, 95% CI=1.74-3.70) and had a previous unilateral therapeutic mastectomy as a treatment for breast (HR=2.69, 95% CI=1.29-5.62).

Contrarily to women who needed less time to decide for RRM, women who deferred RRM were older than 50 years of age, did not have a mother with breast cancer, did not have a previous unilateral breast cancer and had a previous unilateral lumpectomy as a treatment for breast cancer.

Previous studies showed that being a mother¹¹⁻¹³, a previous breast cancer diagnosis^{13,14}, previous mastectomy¹⁵, family history of breast cancer¹⁶⁻¹⁸ and younger age¹⁹ are associated with the decision for RRM. However, how these factors influence the timing of RRM remains unknown⁹. Lodder et al. found it unresolved whether 'young age' or 'having children' is explanatory for the decision for RRM¹². In our study having children or the age of the youngest child are not statistically significantly associated with an earlier decision to undergo RRM in the multivariate model, whereas an age < 50 years predisposes for RRM (HR=2.87 95% CI=1.40-5.92). This can be explained by the fact that we specifically take time to decision into account. A study that also took the time to the decision for RRM into account found similar results; younger than 60 years (HR=1.8, p=0.04) was associated with earlier RRM²⁰. In our study women aged 50 years or over are less likely to choose for RRM than younger women. One of the reasons might be that these women are counselled differently (doctors' factor) counselling concerning RRM than younger women, because of a declining life expectancy gain from RRM with increasing age²². Another explanation could be that these women take their declining risk of breast cancer into account (patient's factor).

Metcalfe et al. found that BRCA1/2 mutation carriers who underwent therapeutic mastectomy as the initial surgery for breast cancer were more likely to undergo contralateral RRM (p < 0.0001)²¹. In another study a statistically significant relation between breast conserving therapy and the decision to undergo contralateral RRM within 1 year of treatment for a primary unilateral breast cancer was found (OR = 1.7, 95% CI=1.21-2.36, p=0.0002)¹⁷. The authors explained this as a relation between failed breast-conserving therapy, followed by RRM. Yi et al. found that there was an association between having one or more relatives with breast cancer and the decision for RRM (OR= 1.57; 95% CI = 1.19-2.09)¹⁸. King et al. also reported the association between having one or more relatives with breast cancer and the decision for RRM (OR = 2.91, 95% CI = 2.33-3.63, p<0.0001)¹⁷. Metcalfe et al. differentiated between different types of relatives (sister, mother). They found that women who had a sister with breast cancer were more likely to undergo RRM (OR=2.4, p=0.003). Women who had a mother with breast cancer also showed a higher uptake of RRM, although this was not statistically significant (OR=1.7, p=0.07)¹⁶. In our study experience with cancer, whether this is personal

experience or experience with affected family members, seem to be a factor closely related to the choice for RRM. It could be that these experiences increase the cancer specific worries²³, which could make women more inclined to choose for RRM to avoid cancer. Another explanation for the relation between experiences with cancer and an earlier decision for RRM is that women are already familiar with the treatment options for breast cancer such as therapeutic mastectomy, thus making the step to RRM easier.

The strength of our study is that the analysis was performed in a large consecutive series of proven *BRCA1* or *BRCA2* mutation carriers, who were counselled in a similar protocolled way by members of one multidisciplinary team. Furthermore, the majority of the data has been collected prospectively and the timing of the decision to undergo RRM is taken into account when analyzing the determinants. Lastly, univariate and multivariate analyses were performed. The fact that this study is quantative in nature is next to strength, also a limitation because qualitative information on underlying motives for RRM is not included. Another limitation is that some data had to be gathered retrospectively when they were missing in the prospective database.

In conclusion, age younger than 50 years, having had a previous breast cancer or having affected family member seem to be factors in an (early) decision for RRM. Therefore, it is advisable to discuss these factors during counselling. The speculations about the underlying motives of women who choose for RRM need to be clarified by longitudinal and qualitative research.

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CHAPTER 3

Quality of Life Outcomes between Mastectomy Alone and Breast Reconstruction. Comparison of Patient-Reported Breast-Q and other Health-Related QoL Measures

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ABSTRACT

Background

Published data on Quality of Life in women after Breast Reconstruction (BR) are inconsistent. This cross-sectional study evaluated the Quality of Life in women after successful breast reconstruction in comparison to those who underwent mastectomy alone.

Methods

The quality of life was evaluated using two validated self-report questionnaires: The Breast-Q and the RAND-36. Demographic information, patient's anxiety, depression and concerns about recurrences were measured by using standardized questionnaires. These questionnaires were sent to the participants. The quality of life of the mastectomy plus breast reconstruction group (n = 92) and the mastectomy alone group (n = 45) were compared. Multiple regression analysis was employed to evaluate the statistical significance of our findings.

Results

Women with successful breast reconstruction were significantly more satisfied with the appearance of their chest / breasts ($p = 0.003$). They also fared better psychosocially ($p = 0.008$) and sexually ($p = 0.007$) than women with mastectomy alone. Furthermore, they functioned better physically ($p = 0.012$), experiencing less pain and limitations ($p = 0.007$).

Conclusions

Successful breast reconstruction following mastectomy can greatly improve different aspects of the patient's life compared to women who do not undergo reconstructive surgery. These findings might be taken into consideration when the treating medical team and the patient study various treatment options.

INTRODUCTION

Breast cancer is recognized as the most common cancer in females worldwide and a leading cause of cancer-related mortality.¹ Despite improvements in screening and diagnosis as well as advances in treatment of breast cancer, mastectomy remains an important surgical option.² Prophylactic Mastectomy (PM) is offered to decrease the risk of gene mutations³, most notably the risk associated with BRCA1 or BRCA2.⁴ However, mastectomy undoubtedly adds a superfluous traumatic burden on the lives of women diagnosed with breast cancer.⁵ Psychological changes may often be detected.⁶ Besides the obvious concerns over physiological health, breast cancer sufferers are also apprehensive about their appearance following a disfiguring operation.⁷ This glum perception may impact their social, personal or sexual relationships.⁸ Half of all women who undergo mastectomy perceive a negative self-image and experience negative changes in their sexuality.⁹ For such women, particularly younger ones for whom physical appearance carries more significance, breast reconstruction, in its various forms, should be considered as a possible solution.¹⁰

A retrospective study by Rowland et al.¹¹ concluded that there were no significant differences in Quality of Life of women who underwent either mastectomy alone, lumpectomy or mastectomy with reconstruction. Only 1/3 of the women however replied to the self-reported questionnaire. Chen et al.¹² concluded that rigorous patient-reported outcomes data are essential and should be the focus of future research. Systematic review by Winters et al.¹³ revealed that most of the studies were poorly designed, retrospective in nature with significant limitations, and potentially biased. Furthermore, the studies were underpowered, and they used generic quality-of-life instruments that were neither sensitive nor specific for breast reconstruction. We may conclude that published data on quality of life in women after breast reconstruction are inconsistent and point out various limitations. The aim of this cross-sectional study was to determine whether successful breast reconstruction improves quality of life in women following mastectomy. For that, we performed a survey among women who underwent surgery for breast cancer at our university hospital and compared the quality of life in women with breast reconstruction to women with mastectomy alone. In addition to the RAND-36, we used the recently published Breast-Q questionnaire to appraise the outcome of breast reconstruction as perceived by the patients themselves.¹⁴ This is currently one of the few instruments in reconstructive breast surgery that meets international standards in terms of development and validation.¹⁵ Naturally, we were also interested in learning of our patients' experiences. This knowledge would empower the future breast cancer sufferers and enable them to make a more informed decision. This decision would rely on an evidence-based protocol designed according to the patient's psychological and social needs.

PATIENTS AND METHODS

Study population

The study population consisted of women who had undergone mastectomy for either breast cancer or prophylaxis due to genetic predisposition. These patients were treated at University Medical Center Groningen between 2006 and 2010. The patients selection procedure is shown in figure 1. The study population consisted of two groups of women: mastectomy alone and mastectomy with successful breast reconstruction. We received approval from the Medical Ethics Committee before conducting the study.

The inclusion criteria included female breast reconstruction patients, mastectomy patients (unilateral or bilateral), patients with good understanding of the Dutch language and signed consent. We excluded patients younger than 18 years of age, severely ill patients, women who were legally incompetent, and women who did not sign the consent form, 12 patients were excluded because of flap or prosthesis loss. In these patients, emotional trauma and disappointment were clear. We considered it unethical to ask women with failed reconstruction to answer questions about the new reconstructed breast.

The initial number of patients considered for the study was 301 women- as depicted in the flow diagram, 264 of which were deemed eligible and thus approached to participate in the study. Out of 264 patients, 139 women had undergone mastectomy and a breast reconstruction whilst 125 women had only mastectomy performed. We received signed informed consent received from 149 subjects, nonetheless 12 were still excluded as detailed in flow diagram. Thus, a total of 137 patients with completed questionnaires and consent form were included: 92 subjects with breast reconstruction and 45 in the mastectomy alone group

Methods

Clinical data was retrieved using digital patient recording by PoliPlus software (Poliplus Software, Waterloo, Ontario, Canada). Where necessary we turned to paper-based documentation. Demographic information (Table 1) such as employment, educational level, marital status and the time interval since last treatment were obtained using the demographic questionnaire formerly used in the Van den Beuken-van Everdingen et al study.¹⁶ In addition, all patients filled in the Hospital Anxiety and Depression Scale^{17, 18} and a Dutch language version of the Concerns About Recurrence Scale.¹⁹ The Hospital Anxiety and Depression Scale appears to be a good assessment of anxiety disorder (Cronbach's alpha = 0.68-0.93) and depression (Cronbach's alpha = 0.67-0.90).¹⁸ While the Dutch Language version of the Concerns About Recurrence Scale measures the influence of fear of cancer recurrence on the Quality of Life in women with breast cancer.¹⁹ Co-morbidities noted included diabetes mellitus, fibromyalgia, hypertension, and psychological instability. American Society of Anesthesiologists classification was noted. In addition, we used tumor, node, metastasis staging. To further condense our population we divided the tumors into two categories: Stage 0 - IIB "and" Stage

Figure 1. Patients selection flow diagram

III - IIIC. Two self-reported questionnaires were used to measure the Quality of Life in our patients: the Breast-Q and the RAND-36.

Table 1. Characteristics of the study population. Based on treatment indication.

Characteristics	Prophylactic Mastectomy alone (%)	Reconstruction Following Prophylactic Mastectomy (%)	Therapeutic Mastectomy alone (%)	Reconstruction Following Therapeutic Mastectomy (%)
No	2	26	43	66
Age at questionnaires completed	50.5 (50-51)	43.0 (26-57)	58.0 (40-76)	50.0 (26-78)
Age at mastectomy	47 (47-47)	40.5 (25-54)	57.0 (38-74)	45.5 (21-72)
Comorbidity	1 (50.0%)	3 (11,5%)	11 (25,6%)	14 (21.2%)
BMI*	31,0 (31-31)	23,0 (20-34)	24,0 (19-35)	25,0 (18-33)
BMI > 30*	1 (50.0%)	2 (8,7%)	2 (5.0%)	10 (15.2%)
Smoking	1 (50.0%)	7 (26,9%)	13 (31.0%)	14 (21.9%)
Chemotherapy	-	-	25 (58.1%)	35 (53.8%)
Radiotherapy	-	-	19 (46.3%)	26 (40.0%)
Bilateral mastectomy †	2 (100%)	26 (100%)	5 (11,6%)	17 (25.8%)
TNM staging ‡				
Stage 0 – IIB	-	-	33 (78.6%)	46 (79.3%)
Stage IIIA – IIIC	-	-	9 (21.4%)	12 (20.7%)
BRCA 1 of 2	2 (100%)	23 (88,5%)	3 (7.0%)	12 (18.2%)
Time between the last operation and completing the questionnaires	37.5 (28-47)	27.0 (5-48)	27,0 (11-45)	24.0 (4-52)
Education:				
Low	2 (100%)	14 (56.0%)	22 (52.4%)	43 (65.2%)
High	0	11 (44.0%)	20 (47.6%)	23 (34.8%)
Family status§:				
Single	1 (50.0%)	2 (8.0%)	8 (18.6%)	12 (18.2%)
Partner	1 (50.0%)	23 (92.0%)	35 (81.4%)	54 (81.8%)
HADS 1	0 (0,0%)	3 (11,5%)	6 (14,0%)	8 (12.1%)
HADS 2	0 (0,0%)	1 (3,8%)	3 (7,0%)	3 (4.5%)
CARS 1	0 (0.0%)	2 (7.7%)	7 (16.3%)	9 (13.6%)
CARS 2	0 (0.0%)	5 (19.2%)	7 (16.3%)	18 (27.3%)
CARS 3	0 (0.0%)	0 (0.0%)	1 (2.3%)	5 (7.6%)
CARS 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (3.0%)

HADS, Hospital Anxiety and Depression Scale; CARS, Dutch language version of the Concerns About Recurrence Scale.

* At the operation.

† Bilateral Mastectomy: for therapeutic mastectomy alone, bilateral malignancy, n = 2, and for unilateral malignancy of one breast and prophylactic mastectomy of the other breast, n = 3. For therapeutic reconstruction, bilateral malignancy, n = 3, and for unilateral malignancy of one breast and prophylactic mastectomy of the other breast, n = 14.

‡ Bilateral malignancy is classified as stage IIIA to IIIC; high education means (university of applied science and university) bachelor's degree and higher; low education is all degrees and levels below bachelor's degree.

§ At completion of the questionnaires.

Breast-Q

The Breast-Q patient-reported outcome instrument is designed to gauge the impact of mastectomy and breast reconstruction on Quality of Life and satisfaction from the patient's perspective. The Breast-Q reconstruction module (postoperative) consists of nine scales. The Breast-Q mastectomy module (postoperative) consists of five scales. Each scale consists of three to five items. The score from each scale is transferred into a 100-point scale. Thus, each scale displays a score from 0 (very dissatisfied) to 100 (very satisfied). The Breast-Q reconstruction module has good internal consistency (Cronbach alpha, 0.88 -0.97)²⁰. The Breast-Q mastectomy module was only recently released. However, we understand that this is similar to the reconstruction module. Before commencing the study, the questionnaires had a Dutch translation validated in accordance with the agreement with the MAPI Trust (<http://www.mapi-trust.org/>). The translated version was approved by Pusic, the author of the Breast-Q.

RAND 36-Item Health Survey

RAND-36 questionnaire consists of 36 items to assess various topics related to health and Quality of Life concentrated under eight domains: physical functioning, physical role functioning, emotional role functioning, vitality, mental health, social role functioning, bodily pain, general health. The Dutch translation has been validated²². The internal consistency of the domains is high (Cronbach's alpha = 0.71-0.92).

Statistical Analysis

To present baseline characteristics, we distinguished the following groups of women: prophylactic mastectomy alone, reconstruction following prophylactic mastectomy, therapeutic mastectomy alone, and reconstruction following mastectomy. We used the medians and ranges or proportions. Multivariate analysis made a distinction between mastectomy alone and reconstruction. The data on the Breast-Q and the RAND-36 were presented by means and standard deviations. Differences on the Breast-Q and the RAND-36 between mastectomy alone and reconstruction were tested by using linear regression modeling. For each dimension of the Breast-Q and the RAND-36, we compared mastectomy alone versus reconstruction. To adjust for differences in baseline to each comparison, the covariates as measured at baseline were added, and in case of any significant effect, these covariates were included in the model. In these multiple models, the variables mastectomy and reconstruction were always included. The regression analyses were tested with a 95 percent confidence interval and a 5 percent significance level ($\alpha = 0.05$) (Table 2). The statistical analysis was performed using SPSS version 18.0 (SPSS, Inc., Chicago, Ill.). Lastly, we reviewed all recorded intraoperative and postoperative complications in both groups.

Table 2. Results of the Multiple Linear Regression Analyses for the Breast-Q and RAND-36 for Mastectomy Alone versus Reconstruction*

	Variables†	β	SE	95 % CI for β	
				Lower	upper
Breast-Q					
Satisfaction with breasts‡	None	10.12	3.33	3.53	16.72
Psychosocial well-being‡	None	8.89	3.29	2.39	15.40
Sexual well-being‡	None	11.59	4.26	3.17	20.02
Physical well-being: breast region	Unilateral or bilateral mastectomy; partner	4 . 5 5	2.88	-1.14	10.24
Satisfaction with the surgeon‡	Chemotherapy	11.34	3.02	5.36	17.32
Satisfaction with the medical team	Unilateral or bilateral mastectomy; education	1.99	3.56	-5.05	9.04
Satisfaction with the administration team	Age at completion of questionnaires; education	4.87	4.14	-3.33	13.06
RAND-36					
Physical functioning‡	Comorbidity	7.65	3.00	1.72	13.58
Social functioning	Comorbidity; partner	1.61	3.08	-4.49	7.71
Physical role problem	Time interval between the last operation and questionnaires completed; comorbidity; BRCA mutation	7.47	6.44	-5.28	20.21
Emotional role problem	Comorbidity; TNM staging	-0.07	7.45	-14.86	14.73
Mental health	Partner	2.86	2.53	-2.14	7.86
Vitality	Comorbidity	-1.82	3.11	-7.97	4.33
Pain†	BMI > 30	9.73	3.56	2.68	16.78
General health	Comorbidity	6.05	3.36	-0.60	12.69
Health change	None	-5.44	4.64	-14.61	3.73

β , coefficient for main effect (mastectomy alone)/reconstruction in the model; SE, standard error for ; CL, confidence limits; TNM, tumor, node, metastasis; BMI, body mass index.

* Coded as 0 for mastectomy alone and 1 for reconstruction.

† Variables are the variables included in the model except the main effect (mastectomy alone/reconstruction), age at mastectomy, age at breast reconstruction, age when quality of life reported, period between mastectomy and breast reconstruction in months, time between breast reconstruction and reporting quality of life, mastectomy indication, tumor/node/metastasis classification, comorbidity, body mass index, body mass index > 30, smoking, radiotherapy, chemotherapy, unilateral or bilateral mastectomy, unilateral or bilateral breast reconstruction, BRCA, primary/secondary breast reconstruction, education level, partner, nipple reconstruction, areola reconstruction, complications (asymmetry, scar, seroma, ptosis, wound healing), and secondary corrections.

‡ Statistically significant.

RESULTS

This cross-sectional study compared two cohorts in which 45 women underwent mastectomy alone and 92 women underwent successful breast reconstruction. The overall response rate was 56.44 percent (149 of 264). Only two women preferred to undergo mastectomy alone for preventive indications (Table 1). The median age was 50.5 years at the time of completing the questionnaires. At the time of mastectomy, both subjects were aged 47 years. Both had *BRCA1* or *BRCA2* gene abnormality and both underwent bilateral mastectomy. However, 26 women underwent prophylactic mastectomy and reconstruction. The median age of the patients at the time of completing the questionnaire was 43 years (range, 26 to 57 years). The median age of the patients at the time of mastectomy was 40.5 years (range, 25 to 54 years). Existing comorbidity was noted in 11.5 percent of patients. The median body mass index at the time of reconstruction was 23 kg/m² (range, 20 to 34 kg/m²). All women had a bilateral mastectomy. *BRCA1* or *BRCA2* gene mutation was detected in 88.5 percent of the subjects in the said group.

Forty-three women had mastectomy alone for malignant disease (Table 1). Reconstruction following mastectomy for malignant indications was performed in 66 women. Patients undergoing only mastectomy had a significantly higher median age (58.0 years; range, 40 to 76 years) at the time of completing the questionnaire ($p < 0.001$) than subjects in the breast reconstruction group (50.0 years; range, 26 to 78 years). Also, the age at the time of mastectomy in the former group was significantly higher ($p < 0.001$) (57.0 years; range, 38 to 74 years) than in the reconstruction group (45.5 years; range, 21 to 72 years). Despite some differences in scores between mastectomy-alone and the reconstruction group, neither the Hospital Anxiety and Depression Scale nor the Dutch language version of the Concerns About Recurrence Scale produced any significant results. However, 73 percent of the mastectomy-alone group did not consider reconstruction. No measured variables could explain the higher score of patients with reconstruction on satisfaction with breasts, psychosocial well-being, and sexual well-being (Table 2). Patients with mastectomy alone were less satisfied with their surgeon than breast reconstruction patients, regardless of whether the patients received chemotherapy or not. Breast reconstruction patients had a higher score on physical functioning, regardless of Breast reconstruction patients reported less pain regardless of whether their body mass index was greater than 30 or not. Table 3 details the score of both the Breast-Q and RAND-36 questionnaires. The score for satisfaction with breasts was a mean of 60.3 in the mastectomy-alone group, whereas in the breast reconstruction group this value was statistically significantly higher (70.5; $p = 0.003$). Similarly, the score for psychosocial well-being was a mean of 66.6 in the former group. This value was again statistically significantly higher in the latter group (75.5; $p = 0.008$). Sexual wellness and satisfaction with surgeon also demonstrated statistically significantly higher values in the reconstruction group ($p = 0.007$ and $p < 0.001$, respectively). Other domains did not depict significant differences, as portrayed in Table 3. The scores for subgroups with therapeutic

Table 3. Mean Breast-Q and RAND-36 Patient-Reported Scores

	Mastectomy Alone (SD)	Reconstruction (SD)	p
Breast-Q			
Satisfaction with breasts	60.33 (19.18)	70.46 (17.90)	0.003*
Satisfaction with the results	—	78.39 (19.07)	
Psychosocial well-being	66.62 (18.31)	75.52 (17.92)	0.008*
Sexual well-being	49.42 (19.44)	61.01 (22.39)	0.007*
Physical well-being			
Breast region	71.59 (13.93)	74.57 (16.27)	0.116
Abdomen	—	67.18 (34.96)	
Satisfaction with nipples	—	64.59 (30.34)	
Satisfaction with information	—	71.04 (15.11)	
Satisfaction with the surgeon	80.16 (19.67)	90.35 (15.28)	<0.001*
Satisfaction with the medical team	86.30 (18.24)	86.68 (20.08)	0.577
Satisfaction with the administration team	85.88 (20.70)	86.01 (19.24)	0.242
RAND-36			
Physical functioning	77.33 (21.86)	86.51 (15.34)	0.012*
Social functioning	83.06 (18.69)	85.48 (17.61)	0.603
Physical role problem	71.11 (40.23)	77.96 (34.15)	0.249
Emotional role problem	75.56 (40.45)	80.29 (35.52)	0.993
Mental health	75.11 (15.16)	77.81 (15.57)	0.259
Vitality	65.78 (15.59)	64.73 (18.01)	0.559
Pain	75.37 (21.64)	83.87 (17.28)	0.007*
General health	68.33 (21.40)	75.54 (17.75)	0.074
Health change	62.78 (25.91)	57.26 (25.16)	0.243

*Statistically significant.

indications had similar significant differences in the same areas of the Breast-Q, as in comparison between the mastectomy and the reconstruction groups. Comparing results from the RAND-36 questionnaire, two important domains showed a marked difference between the mastectomy and the reconstruction groups. Both physical functioning and pain domain scores were better with breast reconstruction. These results were statistically significant ($p = 0.012$ and $p = 0.007$, respectively). In other areas, striking differences were not observed between the two groups, as detailed in Table 3. We looked at complications (e.g., bleeding, seroma formation, delayed wound healing) associated with mastectomy itself. The incidence of such complications was comparable between the two groups. However, as expected, additional complications were identified directly as a result of breast reconstruction. The most notable complications were related to the anastomosis, partial or total flap necrosis, and the loss of prosthesis. In total, 12 patients (7.9 percent) were excluded because of flap loss (five patients) and implant loss (seven patients).

DISCUSSION

Women with breast reconstruction were significantly more satisfied with the appearance of their chest / breasts ($p = 0.003$). They also fared better psychosocially ($n = 0.008$) and sexually ($p = 0.007$) than women with mastectomy alone. Furthermore, they functioned better physically ($p = 0.012$), experiencing less pain and limitations ($p = 0.007$).

Mastectomy is potentially a very traumatic event. Besides immediate concerns over health and longevity associated with breast cancer, patients most likely agonize over their future appearance, social interactions and sexual life. For these women breast reconstruction is proposed as a possible solution. In this study we investigated whether there was a difference in satisfaction and Quality of Life between women with mastectomy alone and women with mastectomy and successful breast reconstruction. Among the self-report questionnaires, the Breast-Q in particular added extra strength to this study, as it is currently the only validated, condition-specific instrument for breast reconstruction surgery.

A previous systematic literature review by Lee et al.²³ could not find any evidence of disparity in satisfaction between patients with mastectomy alone and those undergoing breast reconstruction. However, they do point out the various limitations associated with most studies which make it very doubtful whether the above conclusion is justified. The results from our questionnaires do conclude that women with breast reconstruction are more satisfied with their appearance than women with only a mastectomy. They are also more content with their psychosocial and sexual well-being. Physical functioning in women following breast reconstruction was superior to those with a mastectomy alone. Furthermore, they also experienced less pain and disability. These observations emphasize our propo-

sition that breast reconstruction does facilitate breast cancer sufferers to better cope with various aspects of their lives following completion of their treatment.

In general, women with breast cancer surgery are content with the medical care they receive. However, in our study breast reconstruction patients were more satisfied with their breast surgeon than women with mastectomy alone. Nonetheless this discrepancy may be due to the fact that comparison is being drawn between possibly two different sub-specialties and at different stages of breast cancer treatment. A systematic review by Guyomard et al.²⁴ has reported high satisfaction rates with breast reconstruction, but the authors advised that more robust and evidence based research is needed with validated Quality of Life measures.

Whether unilateral or bilateral breast reconstruction was undertaken also influenced the results in various domains in the Breast-Q. This can be explained by the possible resultant asymmetry. Waljee et al.²⁵ drew a similar conclusion underpinning the importance of breast symmetry or the lack of it in psychosocial functioning of breast reconstruction recipients.

Educational level also correlated with satisfaction of the overall outcome. In our study women with low educational background were more satisfied with the outcome than women with higher education. Similar findings were reported by Medina-Franco et al.²⁶ Perhaps patients with higher education have a higher expectation from breast reconstruction procedures.

We found that chemotherapy affected the Breast-Q score. Although the comorbidity affected the RAND-36 scores, patients with reconstruction had a higher score on physical functioning. Patients who were overweight (body mass index > 30) and underwent reconstruction reported less pain. Lower quality of life is associated with the presence of other diseases. This may be explained by the fact that those parts of questionnaires focused on the overall picture of the patient's condition; they were not designed specifically for breast reconstruction surgery.

This study has some limitations. To begin with bias by indication, the reconstruction technique and study population were not randomized. However, randomization would have been difficult, because it is the patient who will make the decision on reconstruction. We identified only two BRCA patients, who chose to undergo mastectomy alone without reconstruction. Therefore, we decided to include prophylactic and therapeutic mastectomy patients in one group. However, we carried out univariate and multivariate regression analysis to control for the differences in our population. The sample size was not sufficient to control for all biases. However, the power of the outcome "satisfaction with breasts was 80 percent. A total of 115 women chose not to participate in this study. Their reasons and their characteristics were not clear. We cannot exclude that the non participation might have influenced the findings in this study. The low response rate (56.44 percent) could be a potential selection bias. Furthermore, we excluded 12 patients who had flap or implant loss. However, features of failed breast reconstruction patients did not match the features of the breast reconstruction group. The Breast-Q is a condition-specific instrument, and the reconstruction module measures satisfaction with questions about the breast (e.g., softness, size, implant). We found

it inappropriate to ask women those questions after such a traumatic event. The quality-of-life study of Bellino et al.²⁶ excluded patients with cancer recurrences and subjects with breast reconstruction complications. Zhong et al.²⁷ reported a 20 percent rate of major postoperative complications, but no flap loss. After adjusting for complications, the gains in satisfaction with breast, psychosocial well-being, and sexual well-being remained significant.

The study reflects findings from a single institution treating a homogenous population. However, “homogenous population” can be considered as an advantage. In contrast, a multicenter study targeting various ethnic groups would add weight to our findings. Furthermore, we had little information on the emotional background of our patients. The median time between surgical intervention and completion of the questionnaires was 24 months (range, 4 to 52 months). The analysis showed that the time effect was not significant. The retrospective nature of our study could not possibly record the likely variations in perceived quality of life over time. Some women are still in the process of nipple reconstruction or nipple tattooing or are awaiting secondary correction. However, nipple reconstruction showed a positive effect on satisfaction. Previous studies have revealed that the time elapsed since surgery influences the quality of life in women with breast surgery.^{28,29} Therefore, we currently are conducting a prospective study in which patients periodically complete a questionnaire. Nonetheless, to the best of the authors’ knowledge, the Breast-Q has never been used to evaluate satisfaction and quality of life in patients following mastectomy alone or combined with breast reconstruction. Furthermore, combining the validated Breast-Q with the RAND-36, the Hospital Anxiety and Depression Scale, and the Dutch language version of the Concerns About Recurrence Scale in one study is also unique.

Conclusion

Breast reconstruction, in its various forms, has become an appropriate option offered to women diagnosed with breast cancer. Breast reconstruction may be accomplished in one sitting but more often than not, it is a multistage process. As such, many months may lapse before the final intended aesthetic result is achieved. It may also be associated with additional surgical complications as well as higher costs. However, it is evident that patients do benefit from breast reconstruction following mastectomy. Of course, careful patient selection as well as ample patient education is important in empowering patients to make an informed decision in view of their treatment plan. Larger, more comprehensive studies are needed; nevertheless, results from this study will be helpful to both care providers and patients during that decision process.

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CHAPTER 4

Outcome of Quality of Life for Women undergoing Autologous versus Alloplastic Breast Reconstruction Post- Mastectomy. A Systematic Review and Meta-Analysis

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ABSTRACT

Background

This review aimed to meta-analyze the quality of life of alloplastic versus autologous breast reconstruction, when measured with the Breast-Q.

Methods

An electronic PubMed and EMBASE search was designed to find articles that compared alloplastic versus autologous breast reconstruction using the Breast-Q. Studies that failed to present Breast-Q scores, studies which did not compare alloplastic versus autologous breast reconstruction were excluded. Two authors independently extracted data from the included studies. A standardized data collection form was used. Quality was assessed using the Newcastle-Ottawa scale. The mean difference and 95% confidence intervals (CI) between BR means were estimated for each Breast-Q subscale. Forest plots and the I^2 statistic were used to assess heterogeneity and funnel plot publication bias. The Z test was used to assess overall effects.

Results

Two hundred eighty abstracts were found; 10 articles were included. Autologous breast reconstruction scored significantly higher in the five subscales than alloplastic breast reconstruction. The Satisfaction with Breasts subscale indicated the greatest difference, with a mean difference of 6.41 (95 percent CI, 3.58 to 9.24; $I^2 = 70$ percent). The Satisfaction with Results subscale displayed a mean difference of 5.52. The Sexual Well-Being subscale displayed a mean difference of 3.85. The Psychosocial Well-Being subscale displayed a mean difference of 2.64. The overall difference in physical well-being was significant, with high heterogeneity (mean difference, 3.33; 95 percent CI, 0.18 to 6.48; $I^2 = 85$).

Conclusion

Autologous breast reconstruction had superior outcomes compared with alloplastic breast reconstruction as measured by the Breast-Q.

BACKGROUND

Breast cancer is recognized as the most frequently diagnosed cancer in female patients worldwide¹. Surgical intervention including mastectomy is considered an integral part of and often is essential to favorable therapeutic outcome² in many patients. Furthermore, prophylactic mastectomy is an effective treatment in individuals that have higher risk of developing breast cancer, namely in women with a *BRCA* gene mutation or strong family history of the disease³. Despite its therapeutic benefits, surgical intervention can be both physical and psychologically debilitating, with resultant sexual or body-image tribulation⁴. For such individuals, breast reconstruction may be offered primarily or secondarily⁵, using either Autologous or alloplastic reconstructions techniques⁶.

Both methods have been shown to improve patients' satisfaction with breast(s) and consequently their quality of life (QoL) following mastectomy⁷. It would be helpful to know which BR technique is associated with greater QoL outcomes. Guyomard et al⁸ conducted a literature review but the study was more focused on breast reconstruction and was inconclusive as to superiority of any reconstruction technique and reported methodological deficiencies. Winters et al. drew a similar conclusion after their systematic review, acknowledging that most of the studies reviewed were retrospective, underpowered and with inherent limitations⁹. However, a new era started after Pusic et al. designed the Breast-Q, a Patient Reported Outcome Measure¹⁰. The Breast-Q has the following scales: satisfaction with breasts, satisfaction with results, psychosocial well-being, sexual well-being, physical well-being (chest), physical well-being (abdomen), physical well-being (general), satisfaction with nipples, satisfaction with information, satisfaction with the medical care and satisfaction with plastic surgeon. Each scale displays a score from 0 (very dissatisfied) to 100 (very satisfied).

The primary outcome in this study was the patient reported QoL and satisfaction with reconstructed breast (s), as measured with the Breast-Q¹⁰. This is currently the only instrument in reconstructive breast surgery that meets international standards in terms of development and validation¹¹. An increasing number of researchers and surgeons incorporate the Breast-Q in their studies¹². The Breast-Q has increased the use of patient-reported outcome measures in breast surgery and has provided numerous important insights in its brief existence¹³. The aim of our review was to evaluate which BR technique would give the best improvement in individual quality of life and achieve satisfaction as measured with a by patients-reported outcome. To that end, we reviewed and meta-analyzed the literature to assess the of patient-reported outcome measures of alloplastic versus autologous post mastectomy breast reconstruction as measured by the Breast-Q.

PATIENTS AND METHODS

Search strategy

An electronic literature review was performed to identify publications that evaluated alloplastic breast reconstruction compared to autologous breast reconstruction regarding quality of life and satisfaction with breasts as measured with the Breast-Q on October 24th, 2016. (See Appendix, Supplemental Content 1, which shows electronic searches used for this study). Two search engines, PubMed and EMBASE were used. The search was supported by a trained medical librarian. For an overview of the PRISMA study flow diagram, see Figure 1. The search was updated on November 23rd, 2018. This last EMBASE search found a total of 280 abstracts. However, no new article was eligible to be added.

Appendix, supplemental content 1. Electronic searches

(“Mammaplasty”[Mesh] OR “Breast Implants”[Mesh] OR mammaplast* [tiab] OR mammoplast* [tiab] OR
alloplastic implant* OR breast reconstruct* [tiab] OR diep [tiab] OR deep inferior epigastric perforator[tiab]
OR tram [tiab] OR tmg [tiab] OR breast implant* [tiab] OR breast expan* [tiab] OR Latissimus Dorsi [tiab]
OR Transverse Abdominal Musculocutaneous [tiab] OR Transverse Musculocutaneous Gracilis [TIAB] OR
Superior Gluteal Artery [tiab] OR breast prosthes* [tiab]) AND (Breast-Q* [tiab] OR breast Q* [tiab])

Inclusion and exclusion criteria

All studies which compared autologous and alloplastic breast reconstruction and presented Breast-Q scores as an outcome were included. Autologous breast reconstruction included those patients who underwent a deep inferior epigastric perforator flap, transverse myocutaneous gracilis flap, free or pedicled transverse abdominis muscle flap, superficial inferior epigastric artery flap, or latissimus dorsi flap. Alloplastic reconstruction included those patients who had been treated using a direct implant or tissue expander followed by implant with or without any regional flaps¹⁴. Included were studies in which women had undergone mastectomy for therapeutic or prophylactic reasons.

Excluded were studies which included only one breast reconstruction method, studies that did not present the Breast-Q scores, conference abstracts, letters to the editor and non-English papers, studies related to male breast cancer as well as studies on women after breast conserving therapy.

Study selection

The retrieved citations were imported into Excel. Two medical doctors (Y.E. and I.S.K.T.) independently reviewed all titles and abstracts based on a priori defined criteria. Each title and abstract was studied and if it remained inconclusive

whether a study could be included or not, the full paper of the study was retrieved and studied. In case of any discrepancy, this was discussed with a senior clinician (P.M.N.W.). For a Preferred Reporting Items for Systematic Reviews and Meta-Analyses study flow diagram, see Figure 1.

Data extraction and risk of bias assessment

The same authors (Y.E. and I.S.K.T.) independently extracted data from the included studies for data collection and to evaluate methodological quality. A standardized data collection form was used to collect and classify all the data and characteristics of the included studies. To evaluate the methodological quality of the studies, The Newcastle-Ottawa Scale was applied. Again, in case of any discrepancy, this was discussed with a senior clinician (P.M.N.W.). In five studies satisfying our inclusion criteria, but with limited information or missing data, we contacted the authors with additional questions or a request to provide us with the missing or additional data¹⁵⁻¹⁹. Otherwise, we used the data of three studies¹⁵⁻¹⁷ as presented and discussed possible consequences of missing data. Two studies were excluded because the missing data could not be retrieved^{18,19}.

Data synthesis

The subscale considered the primary outcome was satisfaction with breasts. The other Breast-Q subscales were considered secondary outcomes. For each study the mean difference, the mean difference and 95% confidence intervals between autologous and alloplastic breast reconstruction was estimated for each scale of the Breast-Q and described. If there were at least four studies providing data for a given scale, these mean differences were displayed in a forest plot and pooled under the assumption of homogeneity by a random effect model. Statistical heterogeneity was assessed using the I^2 statistic, which was interpreted as follows: 0-40%: probably not important; 30-60% moderate heterogeneity; 50-90% substantial heterogeneity; 75-100% considerable heterogeneity²⁰. We performed separate analyses on the studies with a minimum follow-up of 12 months for the scales with a high heterogeneity. The definition and distribution of subtype breast reconstruction techniques among both the alloplastic and autologous group and the time between breast reconstruction and administration of the Breast-Q (follow-up) were assessed, as they were assumed to be influencers of clinical heterogeneity. To test the differences between the two techniques, the Z test was used. Statistical significance was considered at $P < 0.05$. Publication bias was assessed using funnel plots for the most frequently used subscale physical well-being and the primary outcome satisfaction with breasts. We also included patient characteristics from studies that might be useful to interpret the Breast-Q scores, assess clinical heterogeneity and compare the patient populations using descriptive statistics. Meta-analyses were performed using Review Manager (RevMan) Version 5.3. (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark)

Figure 1. Flowchart. BR, breast reconstruction

RESULTS

Study characteristics

Literature search identified 280 unique articles, of which 10 studies met our inclusion criteria (see Figure 1). In total, 4,957 patients were enrolled in these 10 studies of which in total 3836 patients filled out the Breast-Q (see table 1)^{15-17,21-26,36}. All studies except two were retrospective, cross-sectional studies, the remaining two were prospective studies. The time between the breast reconstruction and administration of Breast-Q varied widely among the articles included in this review (range, 3 to 84 months). The definition of alloplastic and autologous breast reconstruction varied also among the studies: one study defined latissimus dorsi with implant as autologous breast reconstruction¹⁷ others included latissimus dorsi with implant into the alloplastic group^{16,21}. Most studies did not further specify which sub techniques of breast reconstruction were performed among the alloplastic and or autologous group^{15,16,21,23,26}.

The overall mean age of all patients included in this analysis was 51.4±3.8 years (see table 2). Four studies investigated the age of the breast reconstruction groups and found that women undergoing autologous breast reconstruction (range overall mean: 51 to 52.3) were slightly older in all four studies compared to the women undergoing alloplastic breast reconstruction (range overall mean, 44 to 50). As for body mass index, one study focused specifically on thin patients and therefore the mean body mass index was lower among the patients included in that study (alloplastic: 20.3 kg/m² autologous: 21.2 kg/m²)¹⁷ compared to the patients included in the remaining studies (overall mean range 23.5 to 25.9 kg/m² for the alloplastic group and 26.0 to 30.2 kg/m² for the autologous group). Eight studies reported data on smoking and a large variety in incidence was found among the studies (2.7% to 31.8%). The overall complication incidence was high (15.7% to 46.6%), and was reported in four studies^{15,16,21,22}. Five studies reported complication incidence for autologous vs alloplastic breast reconstruction which mostly showed a higher overall incidence for the autologous group (overall mean range 29.2%-46.6% versus 15.8%-31.1% for alloplastic breast reconstruction)^{7,15,22,25,36}. However, when looking at the percentage of the overall complications that were major or led to reconstructive failure, the percentages were higher among the alloplastic group compared to the autologous group (overall mean range 60% to 83% versus 30% to 60%). The studies included reported major complications as complications for which readmission or surgical exploration was necessary.

Quality assessment

The Newcastle-Ottawa Scale for cross sectional studies measured an average 8 points (7-9) from a maximum score of 13 points, table 1.

Table 1. Articles summary

First Author	Year	Study design	Inclusion criteria	
Santosa et al. ¹⁵	2016	R	Data from patients enrolled in Mastectomy Reconstruction Outcomes Consortium (MROC) Study, from February 2012 to January 2014. Any woman who completed implant-based or autologous reconstruction and had at least 2 years of follow-up from their reconstruction date.	
Dean et al. ¹⁶	2016	R	The Flinders Breast Reconstruction Service, University Hospital, southern area of South Australia. All patients referred to the from January 1st, 2010 till Dec. 2014 complete the Breast-Q, (reconstruction module) As an ideal dataset patient would complete three to four post-operative Breast-Q questionnaires, with one at the__3-month post-op, one between 6 and 9 months, one at 12 months post-reconstruction and one post completion of all reconstructive procedures.	
Johnson et al. ¹⁷	2016	R	Women diagnosed with ductal carcinoma in situ or invasive breast cancer (American Joint Committee on Cancer stage 0-III) between January 1, 2005, and December 31, 2011, underwent mastectomy at North Shore University Health System. Aged 65 years or older at the time of mastectomy. sample of women with similar clinical characteristics who were younger than 65 years was surveyed for comparison	
Weichman et al. ²⁵	2015	R	All patients undergoing breast reconstruction at a single institution between November of 2007 and May of 2012. Preoperative body mass index of less than or equal to 22 kg/m ² , follow-up of at least 6 months.	
Pusic et al. ³⁶	2017	P	Age 18 years or older, undergoing first-time, immediate or delayed, bilateral or unilateral postmastectomy breast reconstruction for cancer treatment or prophylaxis. Completed baseline survey 1-year follow-up since the initial reconstruction Breast cancer diagnosis Undergoing immediate breast reconstruction Completed baseline survey 1-year follow-up since the initial reconstruction	

Exclusion criteria	Participants		Follow up*	Auto- logous BR	Allo- plastic BR	Study quality scale
	Number	Filled out BQ	Months mean (range)			
Those who received latissimus dorsi with and without tissue expander/implant reconstructions; women who received a combination of implant and autologous-based techniques. Who changed their reconstructive technique during enrollment in the study. Those who received immediate reconstruction after mastectomy on one side and delayed reconstruction on the other side. Who did not complete the study's preoperative surveys. Who experienced reconstructive failure	1531	U	24	472 NFS	1059 NFS	8
-	343	47% (n=162)	6	69 NFS	93 NFS	7
-	211	49% (n=103)	60 (12-84)	32 Included combined with implant	71 Implants only	8
Preoperative BMI of greater than 22 kg/m2. Without documented BMI. Lacked 6 months' follow-up. Had a reconstruction with one-stage direct-to-implant reconstruction, pedicled flaps alone, or a combination of pedicled flaps and implants.	273	49% (n=133)	3	25 NFS	108 NFS	8
Previous failed reconstruction attempts. Did not complete a baseline (i.e., preoperative) questionnaire. Who had not completed removal of their TE and exchange for implant at the time of the 1-year questionnaire or who had their exchange procedure less than 3 months before the survey. Patients who had a mixed approach to reconstruction Prophylactic mastectomy. Delayed reconstruction. Did not complete baseline survey Less than 1 year of follow-up. Excluded types of reconstruction Patients in TE/I group did not undergo TE exchange 3 months prior to 1-year survey. Reconstructive failure	1632	73% (n=1183)*	12	493 DIEP 294 PTRAM 75 FTRAM 69 SIE 55 1 yr. follow up: 388	1139 TE 1052 DI 87 1 yr. follow up: 795	9

Table 1. Continued

First Author	Year	Study design	Inclusion criteria	
McCarthy et al. ²⁴	2013	R	Consecutive patients treated between (2003–2008) age 21 years and more history of mastectomy alone, immediate postmastectomy two-stage tissue expander/implant reconstruction, or immediate postmastectomy autogenous tissue flap reconstruction; date of completed mastectomy or reconstruction at least 1 year but no more than 5 years prior; and able to read and complete a questionnaire booklet written in the English language	
Eltahir et al. ²¹	2014	R	Successful BR in UMCG between 2006 and 2010 included women with a good understanding of the Dutch language and signed informed consent.	
Lagendijk et al. ²³	2018	R	Participants were recruited by means of an online survey available from February 12 to March 13, 2017. The survey was available on the website of the Dutch breast cancer association and the social media page of our institute.	
Kuykendall et al. ²⁶	2018	R	BR by a single surgeon between July 2011 and July 2015	
Devulapalli et al. ²²	2018	P	All patients undergoing breast reconstruction performed by three plastic surgeons in our department between November of 2010 and November of 2013. Eligibility criteria included patient age of 18 years or older, awareness of the nature of their malignancy, and ability to read English.	

R = retrospective, P = prospective

NFS = not further specified

DIEP = deep inferior epigastric perforators

TMG = transverse myocutaneous gracilis;

TRAM= transverse rectus abdominis musculocutaneous

Ptram = pedicled transverse rectus abdominis muscle

Exclusion criteria	Participants		Follow up*	Auto- logous BR	Allo- plastic BR	Study quality scale
	Number	Filled out BQ	Months mean (range)			
History of irradiation; delayed postmastectomy reconstruction; combined autologous tissue/implant breast reconstruction; documented local recurrence of breast cancer; and/or history of complex regional pain syndrome.	452	48% (n=215)	30 (12-60)	74 NFS	141 NFS	8
Age younger than 18 years, legally incompetent women, metastasis or severely ill patient, reconstruction failure and women who did not give informed consent	139	66% (n=92)	25 (4-48)	47 DIEP 41 TMG 4 TRAM 1 DIEP + SIEA 1	45 IO 32 LD + I 12 SIEA + I 1	9
Patients that had not undergone surgery (yet) or that had undergone surgery <6 months. Questionnaires contained no data	642	17% (n=110)	60 (36-84)	38 NFS	72 NFS	7
Nipple-sparing mastectomy, delayed reconstruction, radiation therapy, additional flap reconstruction, placement of acellular dermal matrix, and those with incomplete data were excluded. In the DIEP flap group, those with incomplete nipple-sparing mastectomy, delayed reconstruction, radiation therapy, additional flap reconstruction, placement of acellular dermal matrix, and those with incomplete data were excluded. In the DIEP flap group, those with incomplete data	311	31% (n=95)	?	37 DIEP	58 NFS	7
-	382	52% (n=200)	12	118 NFS	75 NFS	7

FTRAM = free transverse rectus abdominis muscle

UMCG, University Medical Center Groningen

SIEA =superficial inferior epigastric artery

LD= latissimus dorsi.

IO = implant only

TE = tissue expander followed by implant

*Follow up = time between reconstructive surgery and administration of postoperative Breast-Q

Breast-Q

In all studies, data were presented for the physical well-being scale of the Breast Q (see table 3). All but two publications^{17,24}, used the satisfaction with breasts, sexual well-being and psychosocial well-being scales. The satisfaction with information and the satisfaction with the plastic surgeon scales were used in only three studies^{21,25,26}. Finally, the satisfaction with the nipples and the satisfaction with medical care scales were used in only two studies^{21,26}.

Outcomes and meta-analysis

On average, autologous BR scored higher on almost all scales (nine out of 10) compared to alloplastic BR, ranging between 59 and 91.7 (Table 3). Overall, the scores on satisfaction with breasts were for both reconstruction techniques good, but not excellent (62.7 to 69.8). The satisfaction with breasts subscale indicated the greatest difference between alloplastic and autologous breast reconstruction and was found significant (mean differences, 6.41, 95% CI; 3.85-9.24; $Z=4.44$; $p < 0.001$) but with high heterogeneity ($I^2=70\%$, $p = 0.002$) (Figure 2). As for satisfaction with results subscale, we found a significantly higher satisfaction in the autologous group compared to the alloplastic (mean difference, 5.52; 95 percent CI; 1.56 to 9.48; $Z = 2.73$; $p = 0.006$), with no heterogeneity ($I^2 = 0$ percent; $p = 0.72$) (Figure 3). The sexual well-being subscale displayed the lowest average scores but significantly higher in the autologous group (mean difference, 3.85; 95 percent CI, 2.35 to 5.35; $Z = 5.03$; $p < 0.001$), with no heterogeneity ($I^2 = 0$ percent; $p = 0.76$) (Figure 4). The same is true for difference in psychosocial well-being subscale (mean difference, 2.64; 95 percent CI, 0.84 to 4.44; $Z = 2.88$; $p < 0.004$), but with little heterogeneity ($I^2 = 23$ percent; $p = 0.24$) (Figure 5). The overall difference in physical well-being subscale was significant (mean difference, 3.33; 95 percent CI, 0.18 to 6.48; $Z = 2.07$; $p = 0.04$) but also with high heterogeneity ($I^2 = 85\%$, $p < 0.001$) (Figure 6). When looking at the rest of subscales; no significant differences were found (range 71 to 92) (See supplementary figure 2, which shows Breast-Q subscales). Funnel plots were made, and for the subscales Satisfaction with Breasts and Physical Well-Being, the funnel plots showed all studies located near the average. (See Supplemental Figure 3, which shows funnel plots of the Physical Well-Being subscale). See Supplemental Figure 4, which shows funnel plots of the Satisfaction with Breasts subscale. The separate analyses on the studies with a minimum follow-up of 12 months for the scales with high heterogeneity did not show different results and therefore follow-up does not seem to explain the high heterogeneity among these scales. (See Supplemental Figure 5 which shows Satisfaction with Breasts studies, with or without minimum follow-up of 12 months). See Supplemental Figure 6, which shows Physical Well-Being for studies with or without minimum follow-up of 12 months.

Figure 2. Satisfaction with Breasts subscale. BR, breast reconstruction.

Figure 3. Satisfaction with Results subscale. BR, breast reconstruction.

Figure 4. Sexual Well-Being subscale. BR, breast reconstruction.

Table 2. Patient characteristics

First Author	Year	Title	Data available	Age ¹	BMI ¹	Smoking ²	
Santosa et al.	2016	Effect of Patient Age on Outcomes in Breast Reconstruction: Results from a Multicenter Prospective Study	overall	494 <45y (32.3%) 803 = 45-60y (52.4%) 234 >60y (15.3%)	26.9	41 (2.7%)	
			aut	-	-	-	
			allo	-	-	-	
Dean et al.	2016	A five year experience of measuring clinical effectiveness in a breast reconstruction service using the Breast-Q patient reported outcomes measure: A cohort study	overall	52 (24-82)	-	107 (31.2%) ³	
Johnson et al.	2016	Advanced Age Does Not Worsen Recovery or Long-Term Morbidity After Postmastectomy Breast Reconstruction	overall	60.1 (24-84)	-	-	
Weichman et al.	2015	Patient-Reported Satisfaction and Quality of Life following Breast Reconstruction in Thin Patients: A Comparison between Microsurgical and Prosthetic Implant Recipients	aut	47.3 (9.3)	21.2 (1.4)	0	
			allo	47.6 (9.9)	20.3 (1.4)	26 (7.4)	
Pusic et al.	2017	Patient-Reported Outcomes 1 Year After Immediate Breast Reconstruction: Results of the Mastectomy Reconstruction Outcomes Consortium Study	aut	52.3 (8.6)	28.9 (5.3)	17 (3.5)	
			allo	48.9 (10.3)	25.1 (5.0)	27 (2.4)	
McCarthy et al.	2013	Chest and Upper Body Morbidity Following Immediate Postmastectomy Breast Reconstruction	aut	52 (25-69)	30.2 (19.3-42.6)	8 (5.7%)	
			allo	50 (26-79)	23.9 (17.3-36.6)	0 (0%)	

	Bilateral	Immediate	Chemo ⁴	Radiation ⁴	Complications ⁵	Comorbidities	Partner ⁶	Education ⁷	Income ⁸
	875 (67%)	1429 (93%)	460 (30%)	273 (17.8 %)		-	-	-	-
	-	-	-	-	220 (46.6%) of which 131 major (60%)	-	-	-	-
	-	-	-	-	270 (25.5%) of which 225 major (93%)	-	-	-	-
	-	53 (33%)	-	-	-	-	-	-	-
	65 (50%)	-	-	-	-	-	93 (72%)	53 (40.8%)	20 (15.3%) ⁹
	31 (62%)	479 (81.5%)	25 (30.9%)	15 (18.5%)	83 (24%) of which 6 reconstructive failure (0.1%)	-	20 (80%)	8 (32%)	0 ¹¹
	125 (55.5%)	1398 (98.1%)	105 (30.1%)	81 (23.1%)	5 (0.1%)	-	66 (61%)	52 (48%)	4 (3.7%) ¹¹
	-	493 (100%)	171 (34.7%)	115 (23.3%)	184 (37.3%) of which 104 major (57%)	-	-	86 (17.5)	149 (13.5%)
	-	1139 (100%)	309 (27.1%)	128 (11.2%)	179 (15.7%) of which 107 major (60%)	-	-	403 (35.5)	116 (24.2%)
	15 (20.2%)	-	29 (39.1%)	x	-	-	-	-	-
	66 (46.8%)	-	85 (60.2%)	x	-	-	-	-	-

Table 2. Continued

First Author	Year	Title	Data available	Age ¹	BMI ¹	Smoking ²	
Eltahir et al.	2014	Which Breast Is the Best? Successful Autologous or Alloplastic Breast Reconstruction: Patient-Reported Quality-of-Life Outcomes	aut	51 (35-78)	26 (20-33)	7 (15.2%)	
			allo	44 (26-62)	23.5 (18-34)	14 (31.8%)	
Legendijk et al.	2018	Patient reported outcome measures in breast cancer patients	overall	55.0 (49.0-60.8)	-	-	
Kuykendall et al.	2018	Unilateral Versus Bilateral Breast Reconstruction Is Less Really More?	Overall ¹⁰	155 <55y (51%) 147 >55y (49%)	86 <24.9 (30%) 202 >24.9 (70%)	-	
Devulapalli et al.	2018	The Effect of Radiation on QoL throughout the Breast Reconstruction Process: A Prospective, Longitudinal Pilot Study of 200 Patients with Long-Term Follow-Up	overall	49.2 (5.3)	27.7 (6.0)	12 (6%)	
			aut				
			allo				

1. age and BMI median with range, or mean with SD
 2. percentage of current smokers
 3. percentage of current and reformed smokers
 4. during and/or after reconstruction
 5. percentage of any/overall complications and fraction of major complications which were classified as: hospital readmission, surgical exploration and reconstructive failure
 6. percentage of women in relationship/married
 7. percentage of women with education >college
 8. percentage of women with annual income <\$50,000
 9. percentage of women with annual income <\$40,000
 10. Overall patient demographics unaccounted for non-response and missing data
 11. Percentage of women with education <\$20,000
- x patients with history of radiation were excluded from study

	Bilateral	Immediate	Chemo ⁴	Radiation ⁴	Complications ⁵	Comorbidities	Partner ⁶	Education ⁷	Income ⁸
	13 (27.7%)	17 (36.2)	23 (48.9%)	20 (43.5%)	14 (29.2%) of which 8 major (57%)	11 (23.9%)	39 (84.8%)	12 (25.5%)	-
	30 (66.7%)	28 (62.2)	12 (29.3%)	6 (13.3%)	14 (31.1) of which 10 major (71%)	6 (13.3%)	38 (84.4%)	22 (50.0%)	-
	-	-	-	-	-	-	-	-	-
	-	-	-	-	33 (11%)	-	-	-	-
	19 (10%)	33 (16,5%)	50 (25%)	51 (25.5%)	-	-	-	-	-
					37 (31%) of which 11 major (30%) 41 (19) % of which 29 major (70%)				

Table 3. Breast-Q scores

First Author	Breast-Q Outcomes											
	Satisfaction with breasts		Satisfaction with results		Psychosocial well being		Sexual well being		Physical well being			
									Chest		General	
	Alloplastic/ Autologous		Alloplastic/ Autologous		Alloplastic/ Autologous		Alloplastic/ Autologous		Alloplastic / Autologous		Alloplastic/ Autologous	
Santosa et al. 2016	63.3 (18)	69.3 (18.8)	-	-	74.6 (19.3)	77.1 (18.4)	54.1 (21.3)	58.7 (21.6)	-	-	77.5 (14,3)	77 (15,1)
Dean et al. 2016.	63.9 (56.35-72.11)	66.9 (62.22-71.63)	-	-	70.5 (61.92-79.66)	73.5 (68.43-78.61)	51.9 (45.12-58.80)	57.2 (51.66-62.73)	72.6 (66.28-78.14)	77.3 (73.70-80.79)	-	-
Johnson et al. 2016	-	-	-	-	-	-	-	-	78.4 (16.5)	-	-	-
Weichman et al. 2016	63.7 (15.2)	73.8 (19.8)	73.1 (19.1)	76 (271)	74.2 (19.1)	82.3 (21.6)	56.7 (21.6)	63.8 (21.7)	-	-	78.8 (14.7)	83.6 (17.8)
Pusic et al. 2017	64 (16.8)	67.8 (17.2)	-	-	71.8 (19)	74.7 (19.2)	53 (21.1)	55.4 (19.8)	76.7 (14.5)	74.9 (15.1)	-	-
McCarthy et al. 2014	-	-	-	-	-	-	-	-	-	-	76.5 (16)	82.5 (15.3)
Eltahir et al. 2015.	65.5 (17.55)	75.2 (17.09)	74.5 (19.98)	81.8 (18.69)	77.2 (18.1)	74 (17.8)	61.1 (24.17)	60.9 (20.82)	-	-	71.9 (15.06)	77.1 (17.11)
Lagendijk et al. 2018	53.8 (16.4)	71.9 (16.4)	-	-	63.5 (19.5)	72.7 (19.1)	52.6 (19.4)	60.2 (19.8)	-	-	64.4 (17.3)	68.1 (16.6)
Devulapalli et al. 2018	62.5	64	68	75	76	74.5	52.8	56	64	79	-	-
Kuykendall et al. 2018	64.5	69.3	71.9	73.6	72.8	77.1	54.3	60	70.3	69.5	-	-
AVERAGE	62.7	69.8	71.9	76.6	72.6	75.7	54.6	59	72.4	75.2	73.8	77.7

Breast-Q Outcomes											
	Abdomen	Satisfaction with Nipples		Satisfaction with information		Satisfaction with the Medical care		Satisfaction with Plastic Surgeon		Satisfaction with office staff	
	Autologous	Alloplastic/ Autologous		Alloplastic/ Autologous		Alloplastic/ Autologous		Alloplastic/ Autologous		Alloplastic/ Autologous	
	-	-	-	-	-	-	-	-	-	-	-
	-	-	-	-	-	-	-	-	-	-	-
	80.5 (15.7)	-	-	-	-	-	-	-	-	-	-
	-	-	-	69.4 (19.3)	75.6 (19.5)	-	-	84.4 (20.8)	89.6 (20.7)	-	-
	74.5 (19.1)	-	-	-	-	-	-	-	-	-	-
	-										
	77.4 (23.9)	63.6 (33.99)	65.3 (27.82)	71.4 (15.78)	70.7 (14.61)	85.8 (22.02)	87.5 (18.22)	88.1 (17.29)	87.5 (18.51)	85.7 (18.57)	86.3 (20.05)
	-	-	-	-	-	-	-	-	-	-	-
	-	-	-	-	-	-	-	-	-	-	-
	-	66.9	54.6	71.1	73.9	93.2	95.9	79.4	86	-	-
	77.5	63.6	59.9	70.6	73.4	89.5	91.7	84	87.7	85.7	86.3

Figure 5. Psychosocial Well-Being subscale. *BR*, breast reconstruction.

Figure 6. Physical Well-Being subscale. *BR*, breast reconstruction.

Satisfaction with Office staff

Satisfaction with Plastic surgeon

Satisfaction with Medical care

Satisfaction with Information

Satisfaction with Nipples

Figure, Supplementary Content 2. Satisfaction with the Breast-Q subscales.

Figure, Supplementary Content 3. Funnel plot: Physical well-being

Figure, Supplementary Content 4. Funnel plot: Satisfaction with Breasts

Satisfaction with Breasts studies included with minimum follow up of 12 months

Satisfaction with Breasts for studies with no minimum follow up of 12 months.

Figure, Supplementary Content 5

Physical well-being for studies with minimum follow-up of 12 months

Physical well-being for studies with no minimum follow-up of 12 months

Figure, Supplementary Content 6

DISCUSSION

This systemic review found superior outcome of the Breast-Q scores in patients who underwent autologous breast reconstruction compared to women undergoing alloplastic breast reconstruction regarding satisfaction with breasts, satisfaction with results, sexual well-being, psychosocial well-being and physical well-being irrespective of the timing of the data collection.

Comparison to literature

When evaluating breast reconstruction, where the primary outcome parameter was satisfaction with breasts, Fracon et al. found similar results to our review and concluded that autologous breast reconstruction leads to higher patient

satisfaction than implant breast reconstruction²⁷. Another study found similar results in favor of autologous breast reconstruction²⁸. Similarly, Alderman et al. using a generic questionnaire found that, patients two years postoperative continued to be more esthetically satisfied with autogenous breast reconstruction compared to expander/implant breast reconstruction²⁹.

The physical well-being subscale showed the lowest difference between the two groups, but was still highest after autologous breast reconstruction, which is remarkable since autologous breast reconstruction in general takes a greater physical strain on women compared to alloplastic breast reconstruction. This could be partly explained by the finding that the autologous group indeed suffers from more minor complications and secondary corrections compared to the alloplastic group. In contrast to this, the alloplastic group has a higher incidence of major complications and reconstructive failure (table 2). Other studies comparing different types of breast reconstruction found similar result^{30,31}. In these, multiple months up to years had elapsed between surgery and filling out the Breast-Q which might have affected the Breast-Q scores.

It is remarkable that the scores of the breast reconstruction women in this meta-analysis are much higher than those that have been collected with aid of the Army of Women amongst 1200 women that had not undergone any form of breast surgery. Their mean satisfaction with breasts normative score using the Breast-Q was 58 ± 18 ³². This finding suggests that women with reconstructed breasts are more satisfied with the appearance of their breasts than women with “normal/natural” breasts. However, it may also be that the two groups are not comparable due to selection bias or cultural differences. Comparing the data found in the included studies to normative data collected with aid of the Army of Women might hold a selection bias, as the women included in the Army of Women do not necessarily reflect the average healthy woman in society. The fact that women with reconstructed breasts score higher on satisfaction with breasts could mean that women appreciate the reconstructed breast more since they have felt the emotional loss of their breast(s) and are grateful for their recovery after breast cancer treatment.

This meta-analysis on the scales on satisfaction with breasts and physical well-being subscales showed high heterogeneity (70% and 85% respectively). No high heterogeneity was found among the remaining subscales i.e., satisfaction with results, sexual well-being and psychosocial well-being. Intrainstitutional studies applied their own technique used by their own surgeon, used their own institutional protocols, and treated their own subset of patients, which may cause differences between practices. Heterogeneity can probably be explained by the different methodologies used between studies. The moment of completion of the postoperative Breast-Q varied strongly among the studies included in our analyses (table 1). The two largest studies^{15,36}, both had fixed follow up for taking the postoperative Breast-Q (1 year and 2 years respectively) in contrast to the other studies which had a range of follow up in which the postoperative questionnaires were taken. Besides that, the distribution of subgroup breast reconstruction techniques varied among studies and were not always specified (table 1). Alloplastic breast recon-

struction can be divided into direct implants or tissue expanders followed by implants. Among the autologous group, there too is a variety of techniques available³³. The quality of life may vary among each breast reconstruction subgroup; and therefore, these different definitions can cause heterogeneity. Patient demographics can also cause heterogeneity³⁴, the focus of each of the included studies was not always primarily quality of life. Some studies focused on weight, others on age and others on the administration of radiotherapy. This can cause demographic variety among the studies included in this review and affect heterogeneity. As for publication bias, the funnel plots (supplementary table 2-3) were both situated around the average which suggests that there is probably no or only little publication bias.

Strengths and limitations

The strength of this meta-analysis lies in its strict work flow and protocol. Furthermore, including only articles in which the Breast-Q was used, provided validated patient reported data. However, this review has several limitations. No randomized controlled trials were found. Depending on different factors, patients or physicians chose one of the two alternative modes of intervention. Thus, we accepted non-randomized comparative studies and case-series. In addition, only 10 studies were deemed eligible. Furthermore, not all studies used all Breast-Q scales. Only subscales with data of a minimum of four studies available were used in meta-analyses and discussed in the results section. The other subscales were added as supplementary data in this review. If all scales had been included in the studies this would have created more consistency and might have changed our findings. Having said that, the authors acknowledge that it is challenging for all BR studies to include all scales instead of focusing on the aim of their studies. Additionally, the definition of mixed breast reconstruction, implant plus flap, varied among the studies: some studies defined it as autologous breast reconstruction and others as alloplastic group. Most studies did not further specify which sub techniques of breast reconstruction were performed. In addition, studies did not report information about institutional practices that would have possibly helped explain some of the heterogeneity found among some subscales. Having said this, we also conclude that these interinstitutional differences were not relevant for the subscales Satisfaction with Results, Sexual Well-Being, and Psychosocial Well-Being, given that the I^2 values for these scales were highly homogeneous. Furthermore, at this moment it is unclear whether women opting for autologous BR are equally satisfied before breast reconstruction compared to women opting for alloplastic breast reconstruction. It is possible that, preoperatively, a significant difference in satisfaction with breasts exists between the two reconstruction groups. Also, the timing of reconstruction might be important in this matter. In women undergoing primary reconstruction their own breast is replaced in one operation by a reconstruction. In secondary reconstruction women have experienced the meaning of missing a breast, possibly resulting in a better postoperative Breast-Q score. Finally, most data included in this review were retrieved through retrospective research which leaves more room for bias.

Implications

This review showed that women scored especially low on sexual well-being and future research should consider focusing more on this topic since this contributes also to the overall quality of life of breast cancer survivors and women in general³⁵. The Breast-Q might not be the most suitable questionnaire to further evaluate this topic, but it is currently the only instrument in reconstructive breast surgery that meets international standards in terms of development and validation. Overall, we believe there is a strong need for more prospective studies with preoperative Breast-Q data to compare to the 6 weeks, 6 months, one year postoperative and after completing reconstruction Breast-Q scores, to see whether changes in satisfaction occur over time. We suggest the following breast reconstruction subgroups are created: alloplastic reconstruction on the one hand and autologous reconstruction using free flaps on the other. Cases in which an implant is combined with a flap should in our view be considered a subtype of alloplastic breast reconstruction. Only then can we truly understand how satisfaction evolves over time and how the highest satisfaction level can be achieved for women undergoing breast reconstruction. We also would like to encourage future studies with prospective data collection and a more detailed description of breast reconstruction techniques used, to obtain more comparable study outcomes.

Conclusion

This review showed that women after autologous breast reconstruction were more satisfied and had higher quality of life compared to alloplastic breast reconstruction.

Those undergoing autologous breast reconstruction scored higher in almost all Breast-Q scales compared with alloplastic breast reconstruction, and the greatest difference was seen in Satisfaction with Breasts (mean difference, 6.41; 95 percent CI, 3.85 to 9.24; $I^2 = 70$ percent). Prospective research implementing preoperative questionnaires using all Breast-Q scales is sorely needed to provide more conclusive evidence. Preoperative data give insight into the patient's point of view before surgery and will help assess changes in quality of life over time. Such evidence would assist patients taking their share in the decision on which breast reconstruction procedure would provide them with the highest satisfaction and quality of life after breast reconstruction.

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CHAPTER 5

Which Breast is the Best? Successful Autologous or Alloplastic Breast Reconstruction: Patient-reported Quality of Life Outcomes

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ABSTRACT

Background

Breast reconstruction is an appropriate option offered to women who are diagnosed with breast cancer or gene mutations. It may be accomplished with implants or autologous procedures. This cross-sectional study evaluated the satisfaction and quality of life in addition to complications and secondary corrections in women after successful autologous or alloplastic (implant) breast reconstruction.

Methods

Women were included after successful breast reconstruction. The Breast-Q instrument and standardized questionnaires on depression, recurrence concerns, and anxiety were sent by mail to the participants. In addition, data were collected on complications and secondary corrections. Multiple regression analysis and chi-square tests were applied to evaluate differences between the autologous breast reconstruction group ($n = 47$) and the implant breast reconstruction group ($n = 45$).

Results

Women with a successful autologous reconstruction were significantly more satisfied with their reconstructed breasts than women with successful alloplastic breast reconstruction as measured with the Breast-Q satisfaction with breasts module ($p = 0.023$). More women with an autologous breast reconstruction required secondary correction than women with an implant breast reconstruction ($p = 0.012$). Other findings did not differ between the two groups.

Conclusions

Autologous breast reconstruction leads to more satisfaction than does implant breast reconstruction, notwithstanding that women with an autologous breast reconstruction more often required a secondary correction. The study found no ideal breast reconstruction suitable for all patients. However, this study may inform patients and medical teams in making decisions about breast reconstruction. This pilot study indicated several questions that we plan to further investigate in a larger prospective study.

INTRODUCTION

Breast reconstruction has become an appropriate option for women diagnosed with breast cancer, and it has been reported that 17 percent of mastectomy patients choose for Breast reconstruction¹. Breast reconstruction is accomplished in various ways. The National Health Service national database reported immediate breast reconstruction in 67 percent of the BR cases, directly following the mastectomy¹. However, Breast reconstruction is a secondary process (i.e., in 33% of the cases)¹. The main Breast reconstruction are the autologous or alloplastic techniques the last technique is performed in 63 percent of the cases². The alloplastic Breast reconstruction procedure employs tissue expanders or breast implants with or without a flap. Flaps may be local, such as a lateral thoracodorsal or thoracodorsal artery perforator, or regional, e.g., latissimus dorsi muscle. The flap used most frequently for autologous Breast reconstruction is the Deep Inferior Epigastric Perforator Flap. Usually, nipple reconstruction and areolar-complex tattoo complete Breast reconstruction. If necessary, a correction of the contralateral side is done to improve symmetry. Therefore, many months may pass before the final intended aesthetic result of Breast reconstruction is achieved.

Every Breast reconstruction technique is associated with its own surgical complication and cost profile, as well as its own impact on quality of life. Fischer et al.³ concluded that free flap reconstructions required fewer surgical procedures, had lower rates of complications and failures, required fewer clinic visits, and achieved a final, complete reconstruction faster than expander/implant reconstructions. Ohkuma et al. showed that, although the Quality of Life of both groups was significantly improved postoperatively, autologous Breast reconstruction had a lower physical functioning⁴. Cordeiro and McCarthy⁵ found that 95 percent of the patients who had tissue expander/breast implants were satisfied with the results and said they would choose the same reconstruction type again. Satisfaction did not correlate with late complications, but the study was set up without a reference population. Hu et al.⁶ found that patients with a transverse rectus abdominis musculocutaneous flap reconstruction were more satisfied with their breasts than the patients who got implants. We may conclude from the literature that publications on quality of life following the various breast reconstruction techniques used mainly standard instruments and draw ambiguous conclusions. There is a need for studies based on sensitive and condition-specific instruments⁷.

This study aimed to investigate which technique of breast reconstruction, alloplastic or autologous, gives the highest quality of life. For this reason, we surveyed women who experienced a successful Breast reconstruction at our institution. We used the Breast-Q patient-reported outcomes measure as primary instrument to measure the quality of life and satisfaction outcomes⁸. In addition, data on complications and secondary corrections were collected with widely used and validated questionnaires. We envision to use the outcomes of this study to further tailor the Breast reconstruction procedures according to patients' needs. Moreover, the results can help us to reach the best possible patient counseling, treatment and care.

PATIENTS AND METHODS

Study population

We surveyed women who had breast reconstruction after mastectomy at the University Medical Center Groningen (UMCG), Groningen, The Netherlands, between 2006 and 2010, see the flow diagram (Figure 1). The study population consisted of two groups of women: the successful autologous Breast reconstruction group, and the successful implant Breast reconstruction group. A successful Breast reconstruction was defined as having a unilateral or bilateral breast successfully reconstructed. The study included women with a good understanding of the Dutch language and who signed informed consent. The exclusion criteria were age younger than 18 years, legally incompetent women, the presence of metastasis or severe illness, reconstruction failure and women who did not give informed consent. We received approval from the local Medical Ethics Committee for conducting the study.

In the period from 2006 to 2010, Breast reconstruction was performed in 152 women (See figure 1). One hundred and thirty-nine of these women were considered eligible and were asked to participate in the study. We received signed informed consent from 100 women; of them, eight were excluded as detailed in the flow diagram. A total of 92 women completed the questionnaires: 47 patients who had undergone autologous breast reconstruction and 45 patients who had undergone alloplastic Breast reconstruction group.

Methods

The recently published Breast-Q patient reported outcomes measure was used to appraise the outcome of breast reconstruction as perceived by the patients themselves⁹. This is currently one of the few instruments in reconstructive breast surgery that meets international standards in terms of development and validation. The Breast-Q is designed to gauge the impact of breast reconstruction on quality of life and satisfaction from the patient's perspective. The Breast-Q (postoperative) reconstruction module consists of nine scales. Each scale consists of three to five items on the Likert scale. The score from each scale is transformed into a 100 point scale. Thus, each scale displays a score from 0 (very dissatisfied) to 100 (very satisfied). All scales have a good internal consistency (Cronbach's alpha varies from 0.88 to 0.97)¹⁰. Before starting the study, the Dutch versions of the questionnaires were validated in accordance with the protocol of the MAPI Trust (<http://www.mapi-trust.org/>). The back-translated versions were approved by A. Pusic, M.D., the author of the Breast-Q. In addition, all patients of this study filled in the RAND 36-Item Health Survey¹¹, Hospital Anxiety and Depression Scale (HADS)^{12,13}, and the Concerns About Recurrence Scale-Dutch language version CARS-DLV¹⁴.

Information such as employment, educational level, marital status, and the time interval since the last treatment (Table 1) was obtained with the demographic questionnaire that was also used in the Van den Beuken-van Everdingen et al. study¹⁵. We retrieved clinical data and treatment stages from the patient files.

Figure 1. Flow diagram

DIEP, deep inferior epigastric artery perforator; *TMG*, transverse myocutaneous gracilis; *TRAM*, transverse rectus abdominis musculocutaneous; *SIEA*, superficial inferior epigastric artery; *LD*, latissimus dorsi.

Table 1. Characteristics of patient groups

Characteristics		Autologous n = 47	Implant n = 45	P-value
Age at questionnaires completed		51,0 (35-78)	44,0 (26-62)	p = 0,001*
Age at mastectomy		45,0 (31-72)	42,0 (21-59)	p = 0,034*
Age at reconstruction		49,0 (31-74)	42,0 (22-59)	p = 0,002*
Time interval in months between the 1st. mastectomy and 1st. reconstruction		21,0 (0-135)	0,0 (6-90) ¶	p < 0,001*
Time interval in months between the last reconstruction and questionnaires completed		26,0 (5-52)	23,5 (4-48)	p = 0,135
Comorbidity		11 (23,9%)	6 (13,3%)	p = 0,213
BMI kg/m ² †		26,0 (20-33)	23,0 (18-34)	p < 0,001*
BMI > 30 kg/m ² †		10 (22,2%)	2 (4,5%)	p = 0,015*
Smokers		7 (15,2%)	14 (31,8%)	p = 0,063
Chemotherapy		23 (48,9%)	12 (29,3%)	p = 0,060
Radiotherapy		20 (43,5%)	6 (13,3%)	p = 0,001*
Mastectomy**:	Unilateral	33 (70,2%)	16 (35,6%)	p = 0,001*
	Bilateral	14 (29,8%)	29 (64,4%)	
Reconstruction:	Unilateral	34 (72,3%)	15 (33,3%)	p < 0,001*
	Bilateral	13 (27,7%)	30 (66,7%)	
TNM staging***:	Stadium 0 – IIB	25 (71,4%)	41 (95,3%)	p = 0,099
	Stadium IIIA – IIIC	10 (28,6%)	2 (4,7%)	
BRCA 1 of 2		9 (19,1%)	26 (57,8%)	p < 0,001*
Reconstruction:	Primary	17 (36,2%)	28 (62,2%)	p = 0,012*
	Secondary****	30 (63,8%)	17 (37,8%)	
Nipple reconstruction		32 (68,1%)	24 (53,3%)	p = 0,147
Areola tattoo		26 (55,3%)	16 (35,6%)	p = 0,057
Education:	Low	35 (74,5%)	22 (50,0%)	p = 0,016*
	High	12 (25,5%)	22 (50,0%)	
Partner#	Single	7 (15,2%)	7 (15,6%)	p = 0,964
	Partner	39 (84,8%)	38 (84,4%)	

BMI, body mass index; TNM, tumor, node, metastasis.

* Significant. † At reconstruction. ** Autologous: unilateral malignancy, n = 33; prophylactic bilateral, n = 6; bilateral malignancy, n = 2; therapeutic mastectomy in one breast and prophylactic mastectomy of the other breast, n = 6. Implant: unilateral malignancy, n = 15; preventive bilateral, n = 20; bilateral malignancy, n = 1; therapeutic mastectomy in one breast and prophylactic mastectomy of the other breast, n = 9.

*** If there was a malignancy in both breasts, the tumor was classified in a higher stage.

**** Of these, five women in the autologous group and nine in the implant group underwent primary reconstruction on one side, and on the other a secondary breast reconstruction. Two women received tissue expander first and subsequently underwent prophylactic mastectomy.

¶ High education means (university of applied science and university) bachelor's degree and higher. Low education is all degrees and levels below bachelor's degree. #When questionnaire was completed.

In addition to the complications that had occurred, this registration included the American Society Anesthesiologists classification and co-morbidities, such as diabetes mellitus, fibromyalgia, hypertension, and psychological instability. Data were collected concerning the complication, its treatment and follow up period.

For analysis, disease progression was classified using TNM staging and divided into two categories: Stage 0 - IIB “and” Stage III - IIIC. Furthermore, complications were classified into three groups, according to the treatment that was given to the patient (i.e., expectative, outpatient intervention, or clinical intervention).

Statistical methods

Descriptive statistics were applied to describe baseline characteristics, for which the patients were stratified according to their autologous or implant breast reconstruction. The Breast-Q scores are presented as means and standard deviations. Differences between the two groups on the Breast-Q and Rand-36 were tested with multiple regression analyses to adjust for bias by indication. Differences between the two groups on the HADS and CARS-DLV were tested with multiple logistic regression analyses. In both analyses, a back-transforming method was applied to identify significant variables, as all the multiple models included the variable “Autologous/Implant”. A p-value of 0.05 was used to indicate significance. The complications were analysed with Mann-Whitney U test, and are presented by reconstruction technique. The statistical analyses were performed using SPSS version 18.0 (SPSS Inc., Chicago, IL, USA).

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RESULTS

The overall response rate was 70 percent (100/139). This cross sectional study compared 47 women who experienced autologous breast reconstruction with 45 women post implant breast reconstruction (Table 1).

Several significant differences were noted. The women with autologous breast reconstruction were significantly older than the women in the implant group (51 years and 44 years, respectively). Furthermore, the autologous group underwent mastectomy and breast reconstruction at a significantly higher age (45 years and 42 years, respectively). In addition, women with an autologous breast reconstruction waited significantly longer (21 months) between the mastectomy and reconstruction, than women with an implant breast reconstruction. Seventy six percent of the implant group had bilateral breast reconstruction, and 58 percent of this group had a *BRCA1* or *BRCA2* gene mutation. In the autologous breast reconstruction group, more women had a high BMI and more women in this group received radiotherapy. Autologous breast reconstructions were mainly unilateral and secondary reconstructions. Implant breast reconstructions were more primary and bilateral. More women with implant breast reconstruction were higher educated (50 percent) than women who had autologous breast reconstruction (26 percent).

Table 2. Breast-Q scores

	Autologous	Implants
BQ1 = Satisfaction with breasts	75.19 (17.09)	65.51 (17.55)
BQ2 = Satisfaction with the outcomes	81.82 (18.69)	74.53 (18.98)
BQ3 = Psychosocial well-being	73.96 (17.80)	77.18 (18.10)
BQ4 = Sexual well-being	60.89 (20.82)	61.14 (24.17)
BQ5= physical well-being	77.13 (17.11)	71.89 (15.06)
BQ6 = physical well-being: Abdomen	77.35 (23.90)	--
BQ7 = Satisfaction with nipples	65.31 (27.82)	63.62 (33.99)

Breast-Q

The patients reported on their quality of life, measured with the Breast-Q scores as shown in table 2. After adjustment for significant differences between the two patient groups, patients with autologous breast reconstruction scored significantly higher than patients with implant breast reconstruction in the scale ‘satisfaction with breasts’ ($p = 0.023$). In all other scales there were no other significant differences between autologous and alloplastic breast reconstruction. None of the domains of the RAND-36, HADS and CARS-DLV showed significant differences between autologous and implant breast reconstruction after adjustment for relevant variables (Table 3).

The Complication revisions registration (Table 4) showed asymmetry in 54% of women following autologous reconstruction while this was 11% in women with implant breast reconstruction (Table 5). In addition, more women with an Autologous breast reconstruction [$n=47$ (25 percent)] underwent secondary correction than women with implant breast reconstruction [$n=45$ (12 percent)] ($p=0.012$). There were no significant differences in complications between the two groups.

Table 3. Autologous versus Implant: results of multiple linear regression analysis for Breast-Q and RAND-36.

	Variables†	Beta	S.E.	Sig.	95% CL for B	
					Lower	Upper
BQ1= Satisfaction with breasts	Nipple reconstruction	-8.16	3.52	0.023‡	-15.15	-1.18
BQ2= Satisfaction with the outcomes	Age at questionnaires completed; time between first mastectomy & first reconstruction; chemotherapy, education; nipple reconstruction	4.90	4.00	0.226	-3.09	12.89
BQ3= Psychosocial well-being	Nipple reconstruction	4.61	3.73	0.220	-2.80	12.01
BQ4= Sexual well-being	Unilateral or bilateral reconstruction; nipple reconstruction	6.44	5.03	0.204	-3.56	16.45
BQ5= physical well-being: breast region	Unilateral or bilateral reconstruction	-2.60	3.61	0.473	-9.77	4.57
BQ7= Satisfaction with nipples	None	-1.70	7.92	0.831	-17.55	14.15
R1= physical functioning	Comorbidity: BMI, nipple reconstruction	2.13	3.18	0.506	-4.20	8.46
R2= Social functioning	Comorbidity	-1.21	3.64	0.741	-8.44	6.02
R3= physical role problem	Comorbidity; BRCA; nipple reconstruction	5.41	7.58	0.477	-9.65	20.47
R4= emotional role problem	None	-7.39	7.44	0.323	-22.17	7.38
R5= Mental health	Comorbidity; partner; complications	-2.05	2.30	0.467	-7.62	3.52
R6= Vitality	Comorbidity; smoking	0.88	3.78	0.817	-6.63	8.38
R7= Pain	BMI; smoking	2.40	3.91	0.541	-5.37	10.17
R8= general health	Comorbidity; smoking	4.61	3.67	0.212	-2.68	11.91
R9= Health Change	BRCA	9.28	5.63	0.103	-1.90	20.46

CL, confidence limits; BMI, body mass index; TNM, tumor, node, metastasis.

* Coded as 0 for autologous and 1 for implant. Note that BQ6 can only be measured in the autologous group. Beta is the coefficient for main effect (mastectomy alone)/reconstruction in the model; SE is the standard error for beta.

† Variables are the variables included in the model except the main effect (autologous/alloplastic breast reconstruction); age at mastectomy, age at breast reconstruction, age when quality of life reported, time between mastectomy and breast reconstruction in months, time between breast reconstruction and reporting quality of life, mastectomy indication, TNM classification, comorbidity, BMI, BMI >30, smoking, radiotherapy, chemotherapy, unilateral or bilateral mastectomy, unilateral or bilateral breast reconstruction, BRCA, primary/secondary breast reconstruction, education level, partner, nipple reconstruction, areola reconstruction, complications (asymmetry, scar, seroma, ptosis, wound healing), and secondary corrections.

‡ Significant.

Table 4. Classification of complications per reconstructive group

	No.	Autologous (%)	Implant (%)	P-value
No. of patients in the subgroup		14 (29.2%)	14 (31.1%)	
Complication groups:				
1. Temporary disadvantage expectative policy	3	1 (7.1%)	2 (14.3%)	1.000
2. Recovery after outpatient intervention	11	4 (28.6%)	2 (14.3%)	0.648
3. Recovery after clinical intervention	35	9 (64.3%)	10 (71.4%)	1.000

Table 5. Complication revisions

	Autologous (%)	Implant (%)	P-value	Secondary correction		P- value
				Autologous	Implant	
No.	47	45				
Complications:						
Asymmetry	26 (54.2%)	11 (24.4%)	0.003*	22 (84.6%)	8 (72.7%)	0.403
Excess Skin	7 (14.6%)	5 (11.1%)	0.618	7 (100%)	4 (80.0 %)	0.417
Ugly scar	3 (6.3%)	0		3 (100%)	0	

*Statistically significant.

DISCUSSION

In this study, the Breast Q scale ‘satisfaction with breasts’ results showed that women with autologous breast reconstruction were more satisfied with their breasts than women with an implant breast reconstruction ($p = 0.023$). Our data are in support of previous studies^{16,17}. Alderman et al.¹⁸ concluded that women with a transverse rectus abdominis musculocutaneous flap breast reconstruction were in general more satisfied with their breast reconstruction than women with implants. Bresser et al.¹⁹ showed that almost half of the women with implants feel that the reconstructed breast is not hers. The fact that women with an implant breast reconstruction were less satisfied with their breasts might be associated with the high expectations of young women undergoing prophylactic mastectomy and direct implant reconstruction. In addition, 64 percent of the autologous group underwent secondary reconstruction; they might compare their reconstructed breast to the period after mastectomy.

We found no other differences in QoL between autologous breast reconstruction and Implant breast reconstruction. These results were also found in previous

studies^{16,18,20,21}, although these studies did not use a condition specific instrument such as the Breast-Q.

Our study showed that more women with autologous breast reconstruction needed secondary correction, than women with implant breast reconstruction ($p=0.012$). In women with autologous breast reconstruction more asymmetry was observed than in women with implant breast reconstruction ($p=0.003$). The fact that Autologous breast reconstructions were mainly unilateral and secondary reconstructions, might in part explain the need for secondary operations. Mlodinow et al. showed that autologous reconstruction patients experienced a higher rate of overall complications than implant/expander reconstructions, in addition to higher rates of reoperation. This was mainly because perioperative complications included pedicle thrombosis and hematoma²².

The patients in the autologous group were older and underwent mastectomy and breast reconstruction at significantly higher age than the implant breast reconstruction group. The younger age of the prophylactic mastectomy patients might also help to explain the above differences. Moreover, prophylactic mastectomy patients decided more for direct alloplastic breast reconstruction. In addition, breast reconstruction could be delayed for medical reasons, after therapeutic mastectomy. In our study, the autologous breast reconstruction group spent significantly longer time between the first mastectomy and the first reconstruction than the alloplastic group. Previous studies showed that the time elapsed after surgery positively affected the quality of life in women with breast surgery.¹⁷ In our study, the longer time period between mastectomy and breast reconstruction may have contributed to the higher satisfaction that we found in the autologous breast reconstruction group. However, the time interval between breast reconstruction and survey completion was almost the same for both groups, see table 1.

Sixty four percent of the autologous group underwent secondary breast reconstruction. This may have influenced the quality of life and satisfaction outcomes of this group. The study by Contant et al.²³ found that women with primary breast reconstruction, compared this breast with their natural breasts and were more critical than women with a secondary breast reconstruction. This suggests that women undergoing secondary reconstruction were more easily satisfied. Another study also showed that women with a secondary breast reconstruction were more satisfied with sexuality and femininity than women with primary breast reconstruction²⁴. Roth et al.²⁵ concluded that women with primary breast reconstruction experienced more psychosocial and functional limitations experienced than women with a secondary breast reconstruction. Our findings are in concordance with results suggesting that women with autologous breast reconstruction are more satisfied with their breast(s).

Boughton et al.²⁶ showed that the psychological consequences of breast cancer surgery depend on the personality of the individual and not the type of surgery being performed. A study of Franco-Medino et al.²⁷ found that women with benign breast disease have a better physical self-esteem than women with malignant disease. They suggest that the diagnosis of cancer has a bigger impact on the pa-

tient's self-image than the type of surgical procedure. However, this is not valid for the prophylactic breast reconstruction patients. Damen et al.²⁸ showed that 90 percent of the women with a reconstructed breast by means of a deep inferior epigastric perforator flap felt like it was her own breast. In a study by Drazan et al.²⁹, the deep inferior epigastric perforator flap reconstruction is recommended in prophylactic bilateral mastectomy because in the long term it gives a better tissue replacement than breast reconstruction with implants. This might explain our findings that women with autologous breast reconstruction were more satisfied with their breasts than women with an implant.

Drawbacks of this study include its retrospective nature. In addition, neither patients nor the surgical reconstruction methods were randomized. The choice of a breast reconstruction depends on the patient preference, indication, availability of reconstructive options, and the preference of the surgeon. However, even in a prospective study, randomization of patients might not be ethically acceptable, suggesting that our study design is the best available option. Also, the study analyses were controlled for bias.

We were interested to investigate the unilateral and bilateral breast reconstruction satisfaction. However, the sample size was small to stratify Breast-Q by laterality. We excluded women with prosthesis or flap failure. This might be considered as a drawback, but in our opinion, their quality of life is likely to represent features of a different process as compared to patients with a successful breast reconstruction. We did not distinguish between unilateral and bilateral breast reconstruction within the breast reconstruction groups. Yueh et al.¹⁶ states that a unilateral or bilateral breast reconstruction may play a role in the outcome of satisfaction. Psychosocial well-being, sexual well-being, physical well-being, nipples, satisfaction with care and satisfaction with the outcome of the entire breast procedure, were not significantly different between the autologous and implant groups. Most likely our study population was too small to detect significant results and we consider this study a pilot, to prepare for conducting a larger and prospective study.

Conclusions

Women with a successful breast reconstruction are generally satisfied and have a good quality of life. This study investigated which breast reconstruction method is associated with better outcomes according to the patients. An autologous breast reconstruction gives more satisfaction than an implant breast reconstruction. Between the autologous and implant techniques, we found no differences in quality of life. The findings of this study may inform the professional guidance for breast reconstruction. This may help the patients and medical teams in making informed decisions for breast reconstruction. To strengthen the evidence over the satisfaction with the entire breast procedure, it is necessary to perform prospective studies with larger and homogeneous groups.

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CHAPTER 6

Satisfaction with Cosmetic Outcomes of Breast Reconstruction: Investigations into the Correlation between the Patients' Breast-Q Outcome and the Judgement of Panels

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SUMMARY

Objectives

We aimed to determine the relation between breast reconstruction method, patient satisfaction, and surgeon reported cosmetic outcome among women who underwent breast reconstruction after mastectomy.

Study Design

A cross-sectional study of patients treated between 2006 and 2010.

Main Outcome

Women's satisfaction with cosmetic outcomes after breast reconstruction.

Measures

Cosmetic outcomes were evaluated by 1) women using the Breast-Q to rate satisfaction with breasts outcomes, and by 2) an independent panel using the Strasser score. The relationships between the Breast-Q rating, Strasser scores, and breast reconstruction methods, including laterality and timing, were evaluated by Mann-Whitney *U* tests, Spearman's rank correlations, and Wilcoxon signed-rank tests.

Results

Ninety-four women were included. Patients were more satisfied with their breasts if they had undergone autologous, unilateral, or secondary breast reconstruction compared with those who underwent alloplastic, bilateral, or primary breast reconstruction (p-values 0.008, 0.011, and 0.001, respectively). The Strasser system did not reveal significant cosmetic differences, with all breast reconstructions graded as mediocre or poor.

Conclusions

Patient satisfaction with breast outcomes, as measured by the Breast-Q, was as mediocre or poor reflected by the Strasser score. If doctors are to support patients to make informed decisions on the optimal method of breast reconstruction, we need a more sensitive, comprehensive tool reflecting patients' cosmetic outcomes.

INTRODUCTION

Mastectomy has many negative effects on a woman's body image¹ and can result in psychological changes², with fatigue, sleep disturbance, and depression among the associated complaints³. Half of all women who undergo mastectomy develop a negative self-image and experience negative changes in their sexuality¹. Besides the obvious concerns regarding their health, breast cancer survivors also have been found to worry about their appearance following mastectomy, which is undoubtedly a disfiguring operation⁵. These issues have clear effects on social and sexual relationships⁵.

Though morbidity and mortality were once the main concerns of breast cancer surgery, aesthetic satisfaction, as evaluated by the doctor or the woman herself, are increasingly recognized as important goals of breast cancer surgery⁶. Research has shown that women are generally satisfied with the cosmetic outcomes of their surgery⁷ and that both women and doctors are satisfied with the outcomes⁸. However, these studies were limited by failures to include independent reviews of outcomes, which may potentially have led to bias. In another study, the views of participating women were measured with non-validated or self-designed questionnaires⁹. A methodological flaw in the study by Hunt et al. was that aesthetic results were assessed during a telephone interview and patients were only examined, when possible⁷, while Tzafetta et al. did so during a specifically organized clinical interview and examination⁸. In addition to these limitations and differences, no studies have investigated the relationship between a woman's satisfaction with the outcome of breast reconstruction, measured with the Breast-Q and her doctor's evaluation.

In this study, we aimed to determine the relationship between the breast reconstruction method, the patient's satisfaction, and to evaluate cosmetic outcome among women who underwent breast reconstruction after mastectomy. The cross sectional study focused on a specific stage of the whole reconstruction, the stage matching with the time that the patient was asked to fill out a specific module of the Breast-Q.

6

PATIENTS AND METHODS

Study population

We performed a cross-sectional study of women who underwent breast reconstruction following mastectomy at our center, including all eligible women from a previous study¹⁰. We only included those who underwent successful breast reconstruction between 2006 and 2010, those who had a good understanding of the Dutch language, and those who provided signed informed consent. The exclusion criteria were as follows: metastatic disease, severe illness, inability to complete the questionnaire, and failed breast reconstruction due to complications resulting in either flap or prosthesis loss. As compared to our previous study¹⁰, we included

two additional women who underwent alloplastic reconstruction. The study was approved by the medical ethics committee of our institution.

Measurements and procedure

Patient satisfaction was measured by the Breast-Q and cosmetic outcomes were assessed using the Strasser Grading System by an independent panel of laypeople and experts¹¹.

The Breast-Q

The Breast-Q questionnaire was used to assess the effect of mastectomy and satisfaction with breast reconstruction on quality of life from the patient's perspective. For the current analysis, we only used the Breast-Q scales for satisfaction with breasts, nipples, and overall outcome¹².

The independent review panel

We organized a review panel with 12 members who were independent of the surgical reconstruction team. The panel comprised three plastic surgeons, one oncology surgeon, two breast nurses, and three female and three male laypersons.

The Strasser Grading System

The Strasser Grading System was applied to provide an objective and reproducible grading of the aesthetic outcomes^{11,13}. The system includes five subscales that grade malposition, distortion, asymmetry, contour deformity, and scar on 16-point scales. When the result is perfect or no flaws are seen, the score is 0; 1 is the score in case of any noticeable flaw, 5 for an obvious flaw and 15 for an obvious and deforming flaw. All points are added to get a total score ranging from 0 to 75, with an overall score of 0 indicating a perfect result, 1–4 a good result, 5–14 a mediocre result, and 15 or more a poor result.

Photographs

The medical photographer of our department took photographs according to standardized guidelines introduced by Persichetti in 2007¹⁴. A photograph set comprised one front view, two lateral views, and two oblique views. The photographs were entered in a slide show in PowerPoint® (Microsoft®, Groningen, the Netherlands) with all efforts made to hide patients' identities. The study aimed to correlate the esthetic outcome and the patient perceived QoL at two BR time points. Hence, the photographs used, were the photographs taken at the same time that the Breast-Q was filled in by the patient, which was between 4–52 month after the first stage of breast reconstruction.

Procedure

Before the photographic assessments, we provided information to the independent panel on how to use the Strasser Grading System. Each member of the panel was then individually shown photographs on a computer screen in a random or-

der and was asked to score them individually on an online survey. Obtained data were stored in an Excel® (Microsoft®, Groningen, the Netherlands) spreadsheet and saved on a password-protected computer at our institution.

Statistics

The characteristics of patients and their breast cancer, as well as the treatments received, were stratified by type of breast reconstruction (autologous versus alloplastic). Women with a combined implant and flap reconstruction were considered to have undergone alloplastic reconstruction. The Strasser scores by panel members were pooled such that a single Strasser score and range was given for each patient. Median Breast-Q and Strasser scores, with ranges (min–max), were generated for each type of reconstruction (alloplastic versus autologous, primary versus secondary, and unilateral versus bilateral), and compared by Mann–Whitney *U* tests. The distribution of Strasser scores between professional and lay panel members and between male and female panel members were evaluated by Spearman's rank correlations. We performed all statistical analyses using IBM SPSS, Version 22.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Population characteristics

We enrolled 94 women in this study (Figure 1, Table 1), of whom 47 had undergone autologous and 47 had undergone alloplastic breast reconstructions. The average age at reconstruction was 44.4 years (range: 22–74 years). Concerning reconstruction type, there were 41 deep inferior epigastric perforator (DIEP) flaps, 34 breast implants, 12 implants plus latissimus dorsi muscle flaps, and 4 transverse musculocutaneous gracilis flaps. In addition, one patient underwent breast reconstruction using a free transverse rectus abdominis musculocutaneous (TRAM) flap, another in which a DIEP flap on one side and a superficial inferior epigastric artery (SIEA) flap was performed, and one patient in whom an implant was combined with a SIEA flap.

Photographs

Only 91 women had photographs taken because 2 had undergone additional surgical treatment and 1 did not respond to our enquiries (Figure 1). Of the remaining women, 56 underwent bilateral breast and nipple reconstruction, 18 underwent unilateral breast reconstruction without nipple reconstruction, and 17 underwent bilateral breast reconstruction without nipple reconstruction.

Figure 1. Flow Chart

Breast-Q

The number of women per reconstruction, and their mean Breast-Q scores, is displayed in Table 2. The median Breast-Q scores indicate that the overall results were satisfactory. However, women were more satisfied with their breasts if they underwent autologous, unilateral, or secondary breast reconstructions compared with alloplastic, bilateral, or primary breast reconstructions (p-values 0.008, 0.011, and 0.001, respectively).

Table 1. Characteristics of women by reconstruction type, n (%) or median (min-max)

Characteristics		Autologous n = 47	Implant n = 47
Age at mastectomy		45.0 (31–72)	42.0 (21–59)
Age at reconstruction		49.0 (31–74)	42.0 (22–59)
Age at questionnaires completed		51.0 (35–78)	44.0 (26–62)
Interval (months) between mastectomy and the first reconstruction		21.0 (0–135)	45.0 (0 to 90)
Interval (months) between the last reconstruction and questionnaire completion		26.0 (5–52)	23.5 (4–48)
Comorbidity *		11 (23.4%)	6 (12.8%)
BMI at time of surgery		26.0 (20–33)	23.0 (18–34)
BMI >30 kg/m ²		10 (22.2%)	2 (4.3%)
Smoking		7 (14.9%)	14 (30.4%)
Chemotherapy		23 (48.9%)	13 (30.2%)
Radiotherapy		20 (42.6%)	6 (12.8%)
Mastectomy	Unilateral	33 (70.2%)	16 (34.0%)
	Bilateral	14 (29.8%)	31 (66.0%)
Reconstruction:	Unilateral	34 (72.3%)	15 (31.9%)
	Bilateral	13 (27.7%)	32 (68.1%)
TNM staging	Stadium 0–IIB	25 (71.4%)	23 (92.0%)
	Stadium IIIA–IIIC	10 (28.6%)	2 (8.0%)
BRCA1 or BRCA2 positive		9 (19.1%)	28 (59.6%)
Reconstruction:	Primary	17 (36.2%)	29 (61.7%)
	Secondary	30 (63.8%)	18 (38.3%)
Nipple reconstruction		32 (68.1%)	24 (51.1%)
Areola tattoo		26 (55.3%)	16 (34.0%)
Education:	Low	35 (74.5%)	22 (48.9%)
	High	12 (25.5%)	23 (51.1%)
Partner at time of questionnaire	Single	7 (15.2%)	7 (15.2%)
	Partner	39 (84.8%)	39 (84.8%)

Abbreviations: BMI = body mass index; BRCA1 = BRCA1, DNA repair associated gene; BRCA2 = BRCA2, DNA repair associated gene; TNM = TNM Classification of Malignant Tumors; data are condensed and divided into two categories: Stage 0 - IIB "and" Stage III - IIIC.

* Including: diabetes mellitus, fibromyalgia, hypertension, and psychological instability.

Table 2. Comparison of satisfaction and quality overall, stratified for reconstruction type.

Breast Reconstruction	N	%	Breasts (n = 92) *	Outcome (n = 85) *	Nipples (n = 61) *	Strasser score *** (n = 91) **
Total	92	100	70 (27–100)	75 (35–100)	67 (0–100)	11.0 (6.8–18.1)
Alloplastic	45	50	65 (27–100)	75 (35–100)	64 (0–100)	11.5 (6.8–16.2)
Autologous	47	50	77 (37–100)	86 (35–100)	67 (0–100)	10.8 (7.0–18.1)
P-value			0.008	0.089	0.912	0.409
Primary	45	50	65 (27–100)	67 (35–100)	64 (0–100)	9.7 (6.8–18.1)
Secondary	47	50	73 (37–100)	86 (55–100)	67 (0–100)	11.7 (8.0–15.8)
P-value			P = 0.080	P < 0.001	P = 0.452	P = 0.004
Unilateral	49	52.1	75 (34–100)	86 (47–100)	67 (0–100)	11.2 (7.4–16.2)
Bilateral	43	47.9	69 (27–100)	75 (35–100)	64 (0–100)	10.0 (6.8–18.1)
P-value			0.093	0.011	0.354	0.068

Results are given as median and range. P-values are based on Mann–Whitney *U* tests.

* Breast-Q: Items refer to satisfaction with breast, outcome, and nipples on the Breast-Q. Not all women completed all Breast-Q questions.

** Strasser scores there was no Strasser score for three women.

*** The photographs were taken when women completed the Breast-Q

Strasser scores

The details of the panel members and their scores are given in Table 3. The panel rated no breast reconstructions as perfect or good, 86 as mediocre, and 5 as poor. There were no differences in the distribution of Strasser scores between professionals and laypeople ($p = 1.00$) or between men and women ($p = 0.81$). Also, the Strasser scores were not significantly different when comparing alloplastic and autologous breast reconstructions or comparing bilateral and unilateral breast reconstructions (Table 2). However, the secondary breast reconstructions were associated with significantly better Strasser scores than the primary breast reconstructions ($p = 0.004$).

Table 3. Details of the panel members and their Strasser scores for the breast reconstructions

Assessor	Sex	Age	Profession	Strasser score			
				Perfect	Good	Mediocre	Poor
1	Female	43	Administrative staff member	0	0	56	35
2	Female	46	Secretary	1	0	83	7
3	Male	53	Plastic surgeon	0	0	90	1
4	Male	25	Military	0	0	64	27
5	Male	29	Senior reporting and analysis	0	0	88	3
6	Female	23	Student	0	0	86	5
7	Female	40	Specialist breast nurse	0	0	84	7
8	Male	57	Oncological surgeon	0	0	74	17
9	Male	57	Specialist breast nurse	0	0	57	34
10	Male	25	Student	0	0	76	15
11	Male	44	Plastic surgeon	0	0	62	29
12	Male	39	Plastic surgeon	0	0	88	3

Scores were totalled and ranged from 0 to 75 per woman. Perfect, good, mediocre, and poor results were indicated by overall scores of 0, 1–4, 5–14, and ≥ 15 , respectively.

Breast-Q and Strasser scores

The median Breast-Q scores and Strasser scores for each type of breast reconstruction are displayed in Table 4. There were correlations between poor Strasser scores and lower median scores for satisfaction with breasts ($p < 0.001$) and satisfaction with outcomes ($p = 0.012$). Only one patient reporting satisfaction with their nipples had a poor Strasser score. These correlations between the Strasser scores and the 3 Breast-Q scales '*Satisfaction with Breasts*', '*Satisfaction with Outcome*' and '*Satisfaction with Nipples*' are displayed in figure 2. There was a relation between the Breast-Q scale '*Satisfaction with Breasts*' and the aesthetic score assessed with the Strasser System. Also, a similar relation was present between the '*Satisfaction with Outcome*' and the Strasser Score. Furthermore, there was no correlation between the Strasser Score and the Breast-Q scale '*Satisfaction with Nipples*'.

Table 4. Breast-Q scores stratified by Strasser scores (median; min – max)

Strasser score	N	%	Satisfaction with Breasts (n = 89)	Satisfaction with Outcome (n = 82)	Satisfaction with nipples (n = 59)
Mediocre	86	94.5	73 (45–100)	75 (35–100)	67 (0–100)
Poor	5	5.5	43 (34–53) *	61 (35–75) †	0 (0–0) **

* $p < 0.001$,

† $p = 0.012$. Not all women completed all Breast-Q questions or there was no Strasser score.

** Only 1 patient had a poor Strasser score.

Figure 2. The correlation between Breast-Q score and Strasser Score for the 3 Breast-Q scales

Discussion

Overall, we found that the differences in satisfaction among women, as reported by the Breast-Q, were not reflected by the Strasser scores. Indeed, whereas women were generally satisfied with their breasts and the outcomes of reconstruction, the independent panel evaluated all cosmetic outcomes as only mediocre or poor.

Of particular note, poor Strasser scores only correlated with lower median scores for satisfaction with breasts ($p < 0.001$) and satisfaction with outcomes ($p = 0.012$). Although this was disappointing, earlier research indicated a significant correlation between panel-rated and women-rated scores¹⁵. However, women scored differently within the reconstruction subgroups, with the authors concluding that this was related to the sample size. Although the panel in that research found no cosmetic advantage for one type of reconstruction over another¹⁵, our results are consistent with other research^{10,16,17}, by showing that women were more satisfied with autologous than with alloplastic reconstruction ($p = 0.008$). Although women were more satisfied with their outcomes after unilateral than bilateral reconstruction ($p = 0.011$), the difference was not reflected by our panel's rating, which is similar to the results obtained previously using a four-point scale¹⁸. One explanation for this finding is that breast symmetry is more important to patients, with asymmetry after breast-conserving surgery being significantly correlated with poor psychosocial outcomes¹⁹. The inability of the Strasser score to reflect these differences should raise serious doubts about its sensitivity as a tool for measuring outcomes.

Women were more satisfied with their outcomes after secondary breast reconstruction than after primary breast reconstruction in this study ($p < 0.001$). This is logical if we consider that half of all women are reported to experience a negative self-image and negative change in sexuality after mastectomy¹. This was also supported by the panel ratings, with secondary breast reconstructions associated with significantly better Strasser scores compared with primary breast reconstructions ($p = 0.004$). It was notable that many women chose not to complete the full reconstruction in this study, which is at odds with the findings of other research. For example, Elder et al. reported that the major determinant of aesthetic satisfaction was procedure completion²⁰, while Wellisch et al. reported that nipple reconstruction improved overall satisfaction with breast reconstruction²¹. However, our findings are consistent with those of Andrade et al., who showed no benefit to patient satisfaction from adding reconstruction of the nipple-areola complex to breast mound revisions²².

Literature reviews indicate that no well-established, validated, or reproducible scoring systems exist for panels to use when rating aesthetic outcomes after breast reconstruction, emphasizing the need for a reliable scale that can facilitate comparison^{23,24}. Potter et al. advised that size, shape, and symmetry be included in any aesthetic evaluation²³, while Kim et al. recommended the need for objective assessment of breast anatomy to improve the aesthetic evaluation²⁴. Consistent with this argument, Ching et al. stated that the Strasser system had appropriate

Figure 3. Both results were graded as "mediocre."

face and content validity, but that its validity and reliability had not been formally tested²⁵. Notwithstanding the lack of a validated and reproducible scoring system, and because of the downsides of the other scoring systems, we used the Strasser system because it was the best available option. As illustrated in Figure 3, however, we found this system to be rigid and unable to discriminate between some relevant differences.

We discovered that laypeople and professionals rated cosmetic results similarly using this system, which conflicts with earlier studies indicating that laypeople give harsher assessments, that women are more critical than men, and that surgical specialism can influence assessment^{26,27,28}. For example, Dian et al. reported that women and experts rated aesthetic outcomes higher than laypersons²⁹. In other research, Cardoso et al. reported that the background of an assessor can affect their assessment, and that only experienced assessors should be allowed to assess aesthetic outcomes because they had higher inter-rater agreement compared with inexperienced assessors^{27,30}. We disagree with this view because randomly selected laypeople are likely to be more representative of the patient's social network, a position supported by the fact that laypeople and professionals gave similar ratings in this study.

Furthermore, 3D imaging technologies are more and more used especially in cosmetic surgery to help the patient to get an idea of the expected result. In the future, such technology should be used more widely to provide a more objective prediction of the expected outcome. The study of Mailey et al³¹ concluded that the 3D breast imaging system provides a highly reproducible 3D tool for measuring breast volume and simulating breast augmentation. Accuracy of the 3D models can vary up to 30%. Also, Oren et al³² found that 3D analysis provides volumetric data that is of unique value for surgical planning and postoperative analysis. In the future, this development may result in a new approach and in studies comparing women satisfaction to computer aesthetic outcome analysis.

The existing literature also leads to uncertainty as to whether women only, professionals only, or both should judge aesthetic results. Some authors have stated that patient satisfaction is the most important parameter when evaluating aesthetic outcomes^{33,34}, although it is accepted that this is influenced by the preoperative information they receive, their expectations, and their interaction with the surgeon³⁵. Indeed, when considering where the primacy of opinion lies, we should bear in mind the comment by Strasser, that “even a flawless result can be a bad result if the patient's desires are ignored”¹³. Women's expectations, self-reported outcomes, and ultimately their satisfaction, should be considered the most important determinants of a successful cosmetic outcome from breast reconstruction, not our imposed standards of optimal outcome.

This study has limitations, including the fact that the data were retrospective, that the time interval between breast reconstruction and the study was long for some women (2–3 years), the time span between photographs and the reconstructions varied between 1–52 months and that not all women were at the same stage of breast reconstruction. Other limitations include the small sample size of the

subgroups, the fact that data were from a single practice, the fact that we grouped all autologous approaches together. The latter approach was chosen since we consider implants as the most important determinant of short and long-term complications, irrespective of their precise coverage.

Furthermore, this study excluded women with failed reconstruction, due to the fact that their surgical results and psychosocial status do not match with any of our study groups.

However, grouping the surgical approaches and comparing the two main BR options, may be considered an advantage. In addition, our study benefits from having used patient-reported Breast-Q data. A final strength is that the panel represented both the lay and professional communities.

Conclusion

In this study, the Strasser score only partially reflected women's satisfaction with reconstruction, as measured by the Breast-Q. Unfortunately, however, there are currently no better tools for understanding women's preferences or needs. Prospective research is therefore needed to design a more sensitive and comprehensive scoring system for cosmetic outcomes. It is our contention that women should be the final arbiters of preference, and that we need a comprehensive tool that reflects their preference at its heart. The information gained from this scoring system could help doctors to support patients when making informed decisions about the optimal method of breast reconstruction in a truly shared decision-making process.

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CHAPTER 7

Summary and General Discussion

The primary aim of this thesis to investigate women's satisfaction with breast reconstruction (BR), quality of life (QoL), and other patient-reported outcomes after BR and also to compare and understand which BR procedure leads to more satisfaction. For this purpose, the baseline characteristics of 407 *BRCA 1/2* carriers who opted for early risk reducing mastectomy (RRM) were studied following disclosure of their DNA test results. Next, the QoL of the mastectomy combined with BR versus the mastectomy alone group ($n = 92$ versus 45) were compared. The literature was then reviewed, and a meta-analysis was done to assess patient perspectives on alloplastic versus autologous post-mastectomy BR as measured by the Breast-Q¹. Thereafter, we used the Breast-Q in a cohort of 94 patients who were treated between 2006 and 2010 at UMCG. QoL and satisfaction were evaluated to determine which BR technique would yield the best improvement based on the Breast-Q. Finally, the relationship between the BR technique and patient satisfaction was studied to evaluate cosmetic outcomes in those patients.

The Breast-Q tool was designed to study the impact of BR, QoL, and satisfaction outcome from the perspective of the patient. This tool is currently one of the few patient-reported outcome measurements (PROM) that meet the international standards for development and validation. Our studies aimed to generate Breast-Q data, which should help build a good base for shared decision-making and ultimately selecting the best BR technique that is custom-designed for each patient.

In this chapter, the findings from our studies are summarized, and clinical implications and future perspectives are then discussed.

SUMMARY OF OUR MAIN FINDINGS

In **Chapter 2**, the *BRCA* gene mutation patients' characteristics that are associated with decision for earlier mastectomy treated at UMCG were investigated. Proven *BRCA1/2* gene mutation carriers between 1994 and 2011 were prospectively registered. Patient data and characteristics were collected. The relationship between patient data and their decision for risk-reducing mastectomy (RRM) were studied. Four-hundred seven women were included. The results showed that 36% of all women chose mastectomy within five years after their positive DNA tests. The main features associated with mastectomies were ages less than 50 years previous unilateral breast cancer or mastectomy and familial history of breast cancer.

Chapter 3 of this thesis examined whether women who underwent successful BR reported improved QoL and general outcome-related satisfaction compared to those who underwent mastectomy only. In order to assess this question, four questionnaires were used²⁻⁵; the most specific was the newly developed Breast-Q in addition to the more generic 36-item Health Survey (RAND-36)^{2,3}, the Anxiety and Depression Scale (HADS)⁴, and Concerns About Recurrence Scale (CARS-DLV)⁵. Demographic information was also collected. In total, 137 patients were included in a cross-sectional study in which 92 patients had undergone alloplastic or autologous BR, and 45 had undergone only mastectomy. Analysis of the results showed that women with BR were significantly more satisfied with the appearance of their breasts than those in the mastectomy only group. The BR group reported better psychosocial and sexual parameters with respect to QoL aspects. Also, these patients functioned better physically and had less pain and physical limitations.

In **Chapter 4**, a systematic review and meta-analysis are described concerning the existing evidence on women's reported QoL outcomes and satisfaction after autologous BR versus alloplastic BR as measured using the Breast-Q. The literature search identified 280 unique articles of which 10 studies met our inclusion criteria. In total, 4,957 patients were enrolled from these 10 studies. Similar to our own findings in Chapter 5, autologous BR scored higher on almost all Breast-Q scales when compared with alloplastic breast BR, and the biggest difference between the two groups was seen in satisfaction with breasts.

Chapter 5 of this thesis answered our main question: "Which breast is the best?"; in other words, which BR procedure leads to more satisfaction and more improvement in the patient's QoL? Breast-Q PROM data were collected from 47 women after autologous BR and then compared to the 45 women who underwent the alloplastic procedure. Results showed that women with autologous BR were significantly more satisfied with their breasts than the women of the alloplastic group despite the fact that patients who had undergone autologous BR needed more secondary correction than those who underwent alloplastic BR. All other

aspects of QoL were comparable for the two groups.

Chapter 6 presents the results of a 12-person independent panel that used the Strasser score to evaluate the cosmetic results based on post-operative photographs. The relationship between the panel, the Breast-Q satisfaction score, and the BR technique was investigated. Ninety-four women were included in this study. The patient satisfaction with breast outcomes was reported as mediocre or poor based on the Strasser score. It was disappointing to learn that the Strasser system failed to show significant differences in cosmetic outcomes. However, that finding demonstrates the need for a validated and sensitive cosmetic outcome scoring system.

GENERAL DISCUSSION

Autologous BR is the unequivocal answer to the main question in this thesis that asks: “which breast is the best?” (**Chapter 5**). Our systemic review found similar results. The meta-analysis showed that autologous BR had both superior outcomes and better QoL on almost all Breast-Q scales (**Chapter 4**). This information should be emphasized during our BR consultations. Having said that, alloplastic BR still has a prominent role in BR. All possible surgical advantages of alloplastic BR (no additional scars, quicker procedure, and short recovery) and disadvantages (dual stage procedure, short- and long-term complication risks, and revision surgeries) and the PROM of both options should be explained to new patients. After surgical assessment, only well-informed patients will be able to participate in shared decision-making^{6,7,8}. That shared decision is based on women’s opinions, anatomical and surgical options, and personal experiences about self-esteem, sexuality, and body image. The plastic surgeon’s role is to provide precise and full information about BR and guide women through their decision-making process. A study by Webb et al. concluded that adequate BR information helped women manage their expectations, opt for a specific BR option, and improve their level of satisfaction⁸.

Our study in **Chapter 2** showed that women younger than 50 years were more likely to choose RRM. Additionally, various factors were associated with these younger *BRCA1/2* gene mutation carriers. However, the way in which those factors influence the time needed to make a decision is not clear yet⁹. One explanation could be the psychological stress caused by positive gene tests, which accelerated the decision to undergo a mastectomy. Van Driel et al. investigated those factors and found a significant correlation between women’s intention to opt for RRM and women who had children, high perceived-risk, high cancer worry, and high perceived personal control¹⁰. Hagen et al. studied post-RRM and -BR satisfaction in Norway. Despite a 37.7% complication rate, they found a high satisfaction rate and great relief post-RRM¹¹. Also, Casella et al. concluded that patients are

more satisfied and have a higher QoL using the Breast-Q after RRM, and patients reported higher comfort and increased scores at the 2-year follow-up compared to baseline values¹². Therefore, patients' reported satisfaction and QoL outcomes should be explained to *BRCA1/2* gene mutation carriers before they make their decision to undergo regular magnetic resonance imaging (MRI) screening or RRM.

Our study addressing satisfaction in women with or without BR after mastectomy (**Chapter 3**) showed that BR following mastectomy results in significantly more satisfaction with breasts. Furthermore, women's psychosocial QoL and sexuality reports were better than those who underwent mastectomy only. Not all women get a chance to opt for BR following mastectomy. Alderman et al. showed that only 33% of patients were informed by their oncologic surgeon about BR during the presurgical decision-making process for their cancer treatment¹³. Furthermore, Lee et al. concluded that women treated with mastectomy only were not well-informed about BR¹⁴. Additionally, Frisell et al. found that the immediate BR rate varied between 3% and 26% among different regions of Sweden⁶. These significant differences could be explained by the variations in the patient's information, access to plastic surgery in different regions, and the option of plastic surgery contribution to the decision-making⁶.

Also, in the Netherlands, a considerable variation among hospitals was found in post-mastectomy immediate BR (IBR) rates for both invasive breast cancer (mean 17%) and ductal carcinoma *in situ* (DCIS with a mean of 42%) even after adjustment for patient- and tumor-related factors¹⁵. This issue needs to be further addressed and investigated. On behalf of the NABON breast cancer audit group, De Ligt et al. studied the decision-making process involved in immediate BR in the Netherlands⁷. Their analysis showed that IBR likelihood increased by fourteen times when the patients were informed about this procedure. Their conclusion emphasized the positive effects and importance of treatment information in the IBR decision-making process⁷.

The systemic review, **Chapter 4**, and meta-analysis found that the autologous BR was superior to alloplastic BR. Several studies support our review and showed similar results^{16,17}. The systemic review showed women scored especially low on sexual well-being after breast surgery; this issue should be addressed, and future prospective research should study and focus on this topic since this aspect contributes also to the overall QoL of breast cancer survivors and women in general.

In **Chapter 5**, as in the previous chapter, autologous BR scored better than alloplastic BR. A study by Pusic et al. compared both reconstruction options at one year post-operatively and found similar results¹⁸. However, there is no ideal BR that suits all patients. Alloplastic BR studies showed that women experienced high levels of satisfaction and less pain and tightness one year post-operatively¹⁹. Also, Spindler et al. studied the QoL post-bilateral RRM and pre-pectoral implant BR and found high health QoL, satisfaction with the post-operative outcomes as mea-

sured using the Breast-Q, and improved self-esteem²⁰. However, the drawback of our study “Which Breast is Best?” was the number of cases in the study, which was too small to yield significant results in this thesis on some breast-Q scales or for subgroup analysis based on BR, on indications for BR, or subtypes of breast cancer.

The Strasser score system (**Chapter 6**) failed to distinguish between cosmetic outcomes of breast reconstruction. It seems that the Strasser score system is too restricted to detect the difference between aesthetics and reconstruction. It is good to have such an exact scoring system for assessment in aesthetic breast surgery; however, in reconstructive breast surgery the Strasser score seems inadequate to assess BR cases and score them according to the acceptable outcome standards in BR, for example, it is lacking in assessment of the location and size of scars in secondary BR or autologous BR, or the asymmetry after unilateral BR or even sometimes in bilateral BR. These differences are difficult to explain. Three-dimensional (3D) imaging technologies are used more frequently, especially in cosmetic surgery, to help patients obtain an idea of the expected result. Such technology should be used more extensively to provide a more accurate prediction of the desired outcome in the future. However, such a scoring system may still need input from healthcare panels and human judgment. In a study of the 3D scoring system of BR by Godden et al.²¹, a similar conclusion was reached, and the importance of the development of an objective way to report aesthetic BR outcomes was emphasized.

CLINICAL IMPLICATIONS

Most plastic surgical procedures aim to improve QoL, patient satisfaction, and psychosocial health and are associated with minimal mortality and limited morbidity risks. Collecting PROM data is of the utmost importance when a patient is considering plastic surgery. Currently, the Breast-Q is the most reliable and validated patient-reported outcome measure available for breast surgery patients. Furthermore, women who need to undergo breast surgery have the right to be well-informed about all treatment options, including BR. To achieve well-informed decision-making by a patient, a plastic surgeon should be included in the first stages of treatment discussions, either in a multidisciplinary outpatient clinic, during the multidisciplinary case discussion, and/or by referring every patient who needs breast surgery to a plastic surgeon beforehand. The findings of a study by Frisell et al.⁶ support our suggestions. This process will ensure reliable BR information without the bias of other specialties involved in breast cancer treatment. Providing accurate information about BR treatment options should be the primary goal of every breast team regardless of whether a woman chooses BR or not.

Strong, evidence-based patient education is important in empowering patients to make an informed decision for their treatment plan. Therefore, we are of the

opinion that the Breast-Q should be incorporated into the daily routines of all breast care clinics and integrated into the electronic patient file system. All new patients should be asked to complete the Breast-Q before undergoing breast surgery, after the well-established BR treatment stages, and at specific points during a long follow-up period. Only in this way can longitudinal PROM data be collected, which will help us achieve more insight into the patients' perspectives of the results for our patients and help us to deliver better care.

FUTURE RESEARCH

A prospective multicenter trial to investigate the factors associated with the IBR variation between hospitals in the Netherlands is one suggestion to investigate this variation. Furthermore, this thesis was mainly a retrospective study based on the Breast-Q that investigated whether BR improves patient satisfaction and QoL in women following mastectomy with or without BR. Lack of pre-operative baseline data was a major shortcoming of this study. Pre-operative data on sexuality, physical activities, and psychosocial wellbeing of the two BR groups would be essential for correlating the impact of BR and the Breast-Q score outcomes. Furthermore, data from healthy women and women diagnosed with breast cancer are missing. These topics should be the subject of current research:

- At the time of this writing, a study on normative data of healthy women in the City of Groningen has already been conducted and is awaiting publication.
- A prospective study on BR with a follow-up of three years is also underway and about to be completed.

The first study will make it possible to determine satisfaction with the breasts in the normal population. Such data would also help to elucidate QoL changes in women who develop breast cancer.

The second study includes data concerning the Breast-Q (pre-operative) mastectomy module, which collects baseline pre-mastectomy data and data after a breast cancer diagnosis. These data would help us study how satisfaction and QoL change over time.

A larger, multicenter study is needed to fill this gap. Such a study should include a Breast-Q (pre-operative) mastectomy module to obtain the baseline pre-mastectomy data and data after a breast cancer diagnosis. Additionally, a Breast-Q (post-operative) mastectomy module should also be completed. We could then study the impact of mastectomy with a case-specific and -sensitive questionnaire. All pre-operative data would serve as baseline data for the reconstruction groups. Furthermore, the reconstruction Breast-Q module should be administered at all stages of BR. These steps would allow us to compare and investigate the impact of the different steps in BR on QoL and outcome satisfaction. Future studies need

to address the issue of long-term follow-ups. At this stage, we are processing long-term follow-up data from our study population. With such data, we hope to be able to determine changes in the satisfaction and QoL of the different BR methods over time. This process will drive futures studies and yield important results, which will further facilitate women's decision-making.

The Strasser score system is not appropriate for assessing the results of BR and would require modifications to enable researchers to correctly assess BR results and achieve an accurate response. These modifications would require major changes in the Strasser score system, and this potentially new scoring system must be validated according to the international standards. Therefore, future research should focus on developing a sensitive and reliable cosmetic outcome scoring system based on photographs.

Education of future plastic surgeons should emphasize the importance of patients' perspectives after undergoing BR. Currently, the Breast-Q is the most sophisticated breast surgery outcome measurement instrument and should be incorporated into training programs.

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CHAPTER 8

Nederlandse samenvatting

NEDERLANDSE SAMENVATTING

Het hoofddoel van het onderzoek dat geleid heeft tot dit proefschrift was om vast te stellen welke borstreconstructietechniek, alloplastisch of autoloog, leidt tot de hoogste kwaliteit van leven en patiënttevredenheid bij vrouwen na een succesvolle borstreconstructie volgend op een borstamputatie.

Hoofdstuk 1 is de inleiding waarin in het eerste gedeelte de aandoening borstkanker en de geschiedenis van de behandeling van borstkanker wordt beschreven.

Het tweede deel van de inleiding wordt besteed aan de verschillende manieren van borstreconstructie na een borstamputatie (ablatio mammae of mastectomie) en de ontwikkeling van borstreconstructies in de loop der jaren. De verschillende technieken van borstreconstructie komen hier aan bod, waarbij met name het verschil tussen reconstructies met lichaamseigen weefsel (autologe reconstructies) en reconstructies met prothesemateriaal (alloplastische reconstructies) aan de orde komen. Daarnaast wordt de Breast-Q module uitgelegd, een instrument om kwaliteit van leven na borstoperaties te kwantificeren. Ook wordt de beoordeling van het esthetische resultaat van een operatie met behulp van de Strasser-score beschreven. Ten slotte worden het doel en de opzet van dit proefschrift uiteengezet.

In **Hoofdstuk 2** worden de patiëntkarakteristieken onderzocht welke geassocieerd zijn met een risico-reducerende mastectomie (RRM) bij patiënten met een mutatie in het BRCA-gen. Vanwege het hoge life-time risico op het ontstaan van borstkanker bij deze groep patiënten, wordt vaak gekozen voor een preventieve RRM. Veel van de vrouwen die voor deze ingreep kiezen, kiezen ook voor een borstreconstructie. Meer duidelijkheid over de patiëntdata en -karakteristieken bij deze groep draagt bij aan het vergroten van het inzicht in de keuze voor RRM en mogelijk aansluitend borstreconstructie en is derhalve bijdragend aan de vraagstelling van dit proefschrift. Bewezen BRCA-gen mutatie draagsters zijn tussen 1994 en 2011 prospectief geïnccludeerd en patiëntkarakteristieken zijn verzameld. De relatie met de beslissing voor een risico-reducerende mastectomie werd onderzocht onder de 407 geïnccludeerde vrouwen. Hieruit kwam naar voren dat 36% van deze vrouwen binnen 5 jaar na hun positieve DNA test, welke indiceert dat er sprake is van een erfelijke aanleg voor borstkanker, koos voor een risico-reducerende mastectomie. De belangrijkste karakteristieken geassocieerd met deze keuze waren 'leeftijd jonger dan 50 jaar' en 'een positieve familieanamnese voor borstkanker'.

In **Hoofdstuk 3** van dit proefschrift is onderzocht of vrouwen die een succesvolle borstreconstructie ondergingen een verbeterde kwaliteit van leven en patiënttevredenheid rapporteerden vergeleken met vrouwen die alleen een mastectomie ondergingen. Hiervoor zijn 4 vragenlijsten gebruikt; de Breast-Q, de meer algemene Health Survey (RAND-36), de Anxiety en Depression Scale (HADS), en de Concerns About Recurrence Scale (CARS-DLV). In totaal werden 137 patiënten geïnccludeerd in een cross-sectionele studie waarvan 92 patiënten met een alloplastische óf autologe borstreconstructie na mastectomie en 45 patiënten zonder borstreconstructie na mastectomie. Deze studie laat zien dat vrouwen met borst-

reconstructie significant meer tevreden zijn met het uiterlijk van hun borsten dan vrouwen zonder borstreconstructie na mastectomie. Daarnaast hebben vrouwen met borstreconstructie een betere kwaliteit van leven wat betreft psychosociale en seksuele parameters. Verder functioneren deze vrouwen fysiek beter en geven zij aan minder pijn te hebben.

Hoofdstuk 4 is een systematic review en meta-analyse van de kwaliteit van leven en patiënttevredenheid van vrouwen na autologe borstreconstructie ten opzichte van vrouwen na een alloplastische borstreconstructie. De kwaliteit van leven en patiënttevredenheid zijn gemeten met de Breast-Q waaruit naar voren kwam dat een autologe borstreconstructie tot een hogere kwaliteit van leven en hogere tevredenheid leidt bij vrouwen.

De hoofdvraag van dit proefschrift is ‘welke borst is het beste?’. Het gaat dan om een vergelijking van autologe borstreconstructies met alloplastische borstreconstructies.

In **Hoofdstuk 5** geven we antwoord op deze vraag. Hiervoor hebben we Breast-Q data van 47 vrouwen na autologe borstreconstructie en 45 vrouwen na alloplastische borstreconstructie verzameld. Vrouwen met een autologe borstreconstructie zijn postoperatief significant meer tevreden met hun borsten dan vrouwen na een alloplastische borstreconstructie. Dit was ondanks het feit dat vrouwen met een autologe borstreconstructie vaker een tweede operatie moesten ondergaan voor secundaire correcties dan vrouwen met een alloplastische borstreconstructie. Andere aspecten van de kwaliteit van leven waren vergelijkbaar. Als vrouwen de tevredenheid met hun borsten als belangrijkste factor in het reconstructietraject aangeven, dan geeft een autologe borstreconstructie waarschijnlijk dus de beste borst.

In **Hoofdstuk 6** zijn de cosmetische resultaten onderzocht op basis van post-operatieve foto's. Twaalf onafhankelijke personen hebben de foto's gescoord met een Strasser-score. Dit beoordelingssysteem werd toegepast om een objectieve en reproduceerbare beoordeling van de esthetische resultaten te geven. De relatie tussen deze scores, de Breast-Q tevredenheid score en de borstreconstructie techniek is hiervoor geanalyseerd. De foto's van 94 patiënten konden in deze studie worden geïnccludeerd. Het met de Strasser-score beoordeelde cosmetische resultaat was gemiddeld tot slecht in de onderzochte groep. Helaas kon door de beperkingen in de Strasser-score geen significant verschil worden gevonden tussen de verschillende borstreconstructie technieken. We kunnen dan ook concluderen dat er voor toekomstig onderzoek behoefte is aan een gevalideerd en sensitief score-systeem voor de cosmetische uitkomst van borstreconstructies.

Hoofdstuk 7 is de discussie van het proefschrift en beschrijft de toekomstperspectieven.

KLINISCHE IMPLICATIES

De meeste plastisch chirurgische procedures zijn gericht op het verbeteren van de kwaliteit van leven, de tevredenheid van de patiënt en de psychosociale gezondheid en gaan gepaard met minimale mortaliteit en beperkte morbiditeitsrisico's. Het verzamelen van PROM-gegevens is van het grootste belang wanneer een patiënt plastische chirurgie overweegt. Momenteel is de Breast-Q de meest betrouwbare en gevalideerde PROM (door de patiënt gerapporteerde uitkomstmaat) die beschikbaar is voor patiënten na borstchirurgie. Bovendien hebben vrouwen die een borstoperatie moeten ondergaan het recht om goed geïnformeerd te worden over alle behandelingsopties, inclusief de verschillende mogelijkheden van borstreconstructie. Om de patiënt de mogelijkheid te bieden om tot een weloverwogen beslissing te komen met betrekking tot een eventuele borstreconstructie wanneer er een indicatie is voor een borstamputatie, dient reeds bij de eerste fase van behandelbesprekingen een plastisch chirurg betrokken te worden, hetzij tijdens een multidisciplinair polikliniekbezoek, dan wel tijdens het multidisciplinair mammaverleg.

Wij zijn van mening dat de Breast-Q-vragenlijst opgenomen moet worden in de dagelijkse routine van alle borstklinieken en geïntegreerd in het elektronische patiëntendossier. Alle nieuwe borstreconstructie-patiënten moeten worden gevraagd om de Breast-Q in te vullen voordat ze een borstoperatie ondergaan en op specifieke tijdstippen na de BR operatie gedurende een lange follow-upperiode. Alleen op deze manier kunnen longitudinale PROM-gegevens worden verzameld wat ons zal helpen meer inzicht te krijgen in de perspectieven van de patiënt om ons uiteindelijk te helpen betere zorg te leveren.

TOEKOMSTIG ONDERZOEK

Dit proefschrift betreft voornamelijk een retrospectieve studie gebaseerd op de Breast-Q die onderzocht of BR de patiënttevredenheid en KvL verbetert bij vrouwen na een borstamputatie met of zonder BR. Het ontbreken van preoperatieve baselinegegevens was een belangrijke tekortkoming van deze studie. Preoperatieve gegevens over seksualiteit, fysieke activiteiten en psychosociaal welzijn van de twee BR-groepen zouden essentieel zijn voor het correleren van de impact van BR en de resultaten van de Breast-Q-score. Een prospectieve multicenter studie om de factoren te onderzoeken die samenhangen met de IBR-variatie tussen ziekenhuizen in Nederland is een suggestie om deze variatie te onderzoeken. Bovendien ontbreken gegevens van gezonde vrouwen en vrouwen met borstkanker. Het Strasser-scoresysteem is niet geschikt voor het beoordelen van de resultaten van BR en zou aanpassingen vereisen om onderzoekers in staat te stellen de BR-resultaten correct te beoordelen en een nauwkeurig antwoord te krijgen. Deze wijzigingen zouden grote veranderingen in het Strasser-scoresysteem vergen, en

dit potentieel nieuwe scoresysteem moet worden gevalideerd volgens de internationale normen. Daarom moet toekomstig onderzoek zich richten op het ontwikkelen van een gevoelig en betrouwbaar scoresysteem voor cosmetische resultaten op basis van foto's.

De opleiding van toekomstige plastisch chirurgen zou het belang van de perspectieven van patiënten na het ondergaan van BR moeten benadrukken. Momenteel is de Breast-Q het meest geavanceerde meetinstrument voor de uitkomst van borstchirurgie en het zou in trainingsprogramma's moeten worden opgenomen.

CONCLUSIE

Concluderend geeft dit proefschrift inzicht in kwaliteit van leven en tevredenheid bij vrouwen na een succesvolle borstreconstructie. Hiermee kan, afhankelijk van het doel en de persoonlijke omstandigheden van patiënten, bewuster en doelgerichter gekozen worden voor een bepaalde techniek van borstreconstructie zodat meer 'zorg op maat' geleverd kan worden.

APPENDICES

About the Author
Publications
Dankwoord

ABOUT THE AUTHOR

Yassir Eltahir was born on November 18th 1966, in Khartoum, Sudan. As the first son of two teachers, Khadiga Kandawi and Amir Eltahir as well as a brother to 5 siblings. He left Sudan for the United Arab Emirates at the age of seven, when his Father was assigned to a new teaching position in UAE in 1973. Yassir attended school in UAE graduating from high school in 1985, thereafter his search for a medical school to attend finally ended in Pecs, Hungary in 1986. Yassir attended the English teaching program of Pecs Medical University, it was a metropolitan program with international students from an array of backgrounds and cultures from all over the world, this is reflected in his University friends to this day who have gone onto pursue their careers worldwide. He finished medical school on September 25th, 1993, with cum laude. He then immediately kickstarted his dream in specializing to become a surgeon, finishing the Hungarian General Surgery board examination with an excellent pass mark in 1998. Furthering his progression still, he began his Plastic Surgery training and passed the Hungarian Board of Reconstruction, Aesthetic and Burn Plastic Surgery with an excellent mark yet again in February of 2003. Shortly, he was offered a position in a plastic surgery training clinic and started immediately as a board certified Plastic Surgeon. Following this, roughly in that same year he set up a private practice as well with his friend Afshin Dehghani. After considering a Dutch friend's suggestion to take up a plastic surgeon vacancy advertised in UMCG, Yassir decided to apply for the role in 2004 and was consequently accepted, starting his role as a consultant plastic surgeon in UMCG.

After only learning Dutch for 2 weeks he began his role at UMCG and settled in an apartment where he continued teaching himself Dutch for the following year. He dedicated his career in UMCG mainly for Breast reconstruction, aesthetic surgery and in later periods he extended the application of Lotus Petal flap to a bigger defect in the perineal area.

Aesthetic Plastic Surgery is another great passion of his, which he practiced since the early days of his career. In 2015 he joined Bergman Bey Clinics and he managed to hone his skills and build his profile in this field.

He passed the European Board of Plastic Reconstructive and Aesthetic Surgery examination in 2009. During his career, he has attended many courses, congresses, meetings and visited many colleagues in their clinics to gain more experience and a wider scope of understanding of plastic surgery. He is a member of several national and international plastic surgery societies, and (co)author of 16 published plastic surgery articles. Among his many achievements and accolades Yassir was awarded the Best Paper in 2016 by Plastic, Reconstructive Surgery Journal for his article "Which Breast Is the Best?"

PUBLICATIONS

Outcome of Quality of Life for Women Undergoing Autologous versus Alloplastic Breast Reconstruction following Mastectomy: A Systematic Review and Meta-Analysis. **Yassir Eltahir**¹, Irene S Krabbe-Timmerman¹, Nadia Sadok¹, Paul M N Werker¹, Geertruida H de Bock¹. **Plast Reconstr Surg.** 2020 May;145(5):1109-1123

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