Long-Term Health-Related Quality of Life after Four Common Surgical Treatment Options for Breast Cancer and the Effect of Complications: A Retrospective Patient-Reported Survey among 1871 Patients

Casimir A. E. Kouwenberg, M.D., M.Sc.
Kelly M. de Ligt, Ph.D.
Leonieke W. Kranenburg, Ph.D.
Hinne Rakhorst, M.D., Ph.D.
Daniëlle de Leeuw, M.D., M.Sc.
Sabine Siesling, Ph.D.
Jan J. Busschbach, Ph.D.
Marc A. M. Mureau, M.D., Ph.D.

Rotterdam, Utrecht, Enschede, and Almelo, The Netherlands

Background: Differences in quality-of-life outcomes after different surgical breast cancer treatment options, including breast reconstruction, are relevant for counseling individual patients in clinical decision-making, and for (societal) evaluations such as cost-effectiveness analyses. However, current literature shows contradictory results, because of use of different patient-reported outcome measures and study designs with limited patient numbers. The authors set out to improve this evidence using patient-reported outcome measures in a large, cross-sectional study for different surgical breast cancer treatment options.

Methods: Quality of life was assessed through the EQ-5D-5L, European Organization for Research and Treatment of Cancer Quality of Life Questionnaires C30 and BR23, and the BREAST-Q. Patients with different treatments were compared after propensity-weighted adjustment of pretreatment differences. The EQ-5D was used to value the effect of surgical complications.

Results: A total of 1871 breast cancer patients participated (breast-conserving surgery, n = 615; mastectomy, n = 507; autologous reconstruction, n = 330; and implant-based reconstruction, n = 419). Mastectomy patients reported the lowest EQ-5D score (mastectomy, 0.805, breast-conserving surgery, 0.844; autologous reconstruction, 0.849; and implant-based reconstruction, 0.850) and functioning scores of the C30 questionnaire. On the BREAST-Q, autologous reconstruction patients had higher mean Satisfaction with Outcome, Satisfaction with Breasts, and Sexual Well-being scores than implant-based reconstruction patients. Complications in autologous reconstruction patients resulted in a substantially lower quality of life than in implant-based reconstruction patients.

Conclusions: This study shows the added value of breast conservation and reconstruction compared with mastectomy; however, differences among breast-conserving surgery, implant-based reconstruction, and autologous breast reconstruction were subtle. Complications resulted in poorer health-related quality of life. (*Plast. Reconstr. Surg.* 146: 1, 2020.)

From the Department of Plastic and Reconstructive Surgery, Erasmus MC Cancer Institute, University Medical Centre Rotterdam; Department of Research, Netherlands Comprehensive Cancer Organisation; Department of Health Technology and Services Research, Technical Medical Centre, University of Twente; Department of Psychiatry, Section of Medical Psychology and Psychotherapy, Erasmus Medical Center; Department of Plastic, Reconstructive, and Hand Surgery, Hospital Medisch Spectrum Twente/Hospital Group Twente; and Department of Surgery, Hospital Group Twente.

Received for publication March 14, 2019; accepted January 17, 2020.
The first two authors contributed equally to this work.
Presented at the 2018 San Antonio Breast Cancer Conference, in San Antonio, Texas, December 4 through 8, 2018; and the Fall Meeting of the Netherlands Society for Plastic Surgery, in Ede, The Netherlands, November 3, 2018.

DOI: 10.1097/PRS.0000000000006887

Because 5-year survival rates for early-stage breast cancer are relatively high,[1,2] the effects of breast cancer and its treatment on quality of life become more important, which may affect surgical decision-making. Because mastectomy and breast-conserving surgery including radiotherapy have similar disease-free and overall survival,[3–5] the effects of different treatment modalities on outcomes other than survival gain significance. Because loss of a breast may negatively affect psychosocial health, body image, and sexual function,[6] guidelines recommend that the possibility of breast reconstruction should be discussed with every patient scheduled for mastectomy.[7–9] Multiple options are available, either using autologous tissue (autologous breast reconstruction) or breast implants (implant-based breast reconstruction), varying in costs, timing, duration, complication rates, and cosmetic results.[6,10,11] Breast reconstruction aims to improve the patient's well-being and health-related quality of life,[6,10] but patients opting for breast reconstruction also have a risk of complications,[12–15] reconstruction failure,[12,13] or disappointing (cosmetic) results.[6] Consequently, shared decision-making between physicians and patients about the preferred surgical treatment is a complex tradeoff between outcomes and risks.

Health-related quality-of-life outcomes after different surgical breast cancer treatment options are relevant for counseling individual patients in clinical decision-making, and for societal evaluations as cost-effectiveness analyses used in health policy. Research shows that posttreatment health-related quality of life is relatively high in breast cancer patients, but evidence about (differences in) health-related quality of life after different treatment options is conflicting.[16–19] This conflicting evidence may be explained by variation in the use of patient-reported outcome measures, study designs, and patient populations. For instance, there are studies that both have and have not found differences in health-related quality of life between patients who had undergone breast-conserving surgery or mastectomy.[20] Also, several higher quality studies did not find statistically significant differences in health-related quality of life, body image, and sexuality between patients with or without breast reconstruction.[21] We believe that evidence should be improved, as such information is relevant for choosing a treatment in clinical decision-making and for health policy. Until now, outcomes have been generally measured in small, cross-sectional, single-center studies. Ideally, one would include all surgical options relevant to breast cancer patients in one large prospective cohort study.[21] Santosa et al. performed such a large prospective study, comparing patients with implant-based and autologous breast reconstruction.[22] Furthermore, outcomes measured over a longer period would be of interest, as different surgical outcomes may have a different health-related quality-of-life course over time. For example, recovery from surgical complications will take additional time.

To improve the evidence on the impact of breast cancer surgery and consequently for clinical decision-making and health policy, the present study aimed to compare health-related quality-of-life outcomes for four common surgical breast cancer treatment options (i.e., breast-conserving surgery, mastectomy, autologous breast reconstruction, and implant-based breast reconstruction). Health-related quality of life was assessed using multiple patient-reported outcome measures in a large, multicenter, retrospective, cross-sectional cohort of breast cancer patients up to 10 years after diagnosis. The second aim was to investigate the impact of complications on health-related quality of life following these different surgical treatment options. We hypothesized that breast-conserving surgery and autologous breast reconstruction are favorable over implant-based breast reconstruction and mastectomy in terms of health-related quality of life, however, in the absence of complications, with mastectomy yielding the least preferable outcomes.

Disclosure: *Prof. Dr. Busschbach is a member of the nonprofit EuroQoL Group and receives financial compensation for managerial activities for the group. For the remaining authors, no financial interests were declared. No funding was received for this work.*

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PATIENTS AND METHODS

Study Population

Female breast cancer patients ($n = 3804$) from four hospitals in The Netherlands (one academic

hospital and three general hospitals) were invited by mail to participate in a self-administered cross-sectional online survey. Patients were included if they had been surgically treated for nonmetastatic breast cancer in the past 10 years (2008 to 2018). Patients who had developed distant metastases since curative treatment or who were not proficient in Dutch were excluded. Four groups were formed based on the surgical procedure: breast-conserving surgery, mastectomy, autologous breast reconstruction, and implant-based breast reconstruction. Time between surgery and invitation was over 6 months, to ensure patients had recovered from the treatment. Patients who preferred completing a paper questionnaire were sent one on request. Respondents gave informed consent for processing their coded survey results. The Medical Ethics Committee of the Erasmus MC reviewed and approved the study protocol (MEC-2015-273).

Measures

The survey included questions regarding baseline patient and treatment characteristics, including surgical complications, and the following validated questionnaires.

EQ-5D-5L

This questionnaire of health status measures problems in five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), all with five levels of severity (no, slight, moderate, severe, and extreme problems). According to health state, a "value" can be assigned, where 0.00 and 1.00 represent the value for death and perfect health, respectively. This value is also referred to as utility, index score, or preference. The EQ-5D includes values of the general public in the valuation of health-related quality of life, resulting in "preference-weighted quality-of-life scores," often referred to as "utilities." Utilities are used as outcomes in economic evaluations, which can inform health policy. A mean general population reference was obtained to compare study results to that of a sample of the Dutch general population.[23]

European Organization for Research and Treatment of Cancer Quality of Life Questionnaires C30 and BR23

The European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaires measure health-related quality of life in cancer patients,[24] and the breast cancer–specific Quality of Life Questionnaire BR23 supplements the cancer-specific Quality of Life Questionnaire C30.[25] Both consist of functioning and symptom scales; the C30 questionnaire also includes a global health status scale. All items and scales range from 0 to 100, with higher scores presenting a higher level of functioning or general health for the functional and global health status scales, respectively, and higher scores representing a higher level of symptoms for the symptom scales.[26]

BREAST-Q

The BREAST-Q is treatment-specific patient-reported outcome measure, developed to measure breast-related quality of life and satisfaction on several health-related quality-of-life domains. Six postoperative domains were used from the different modules, which were developed for the respective patient groups: Satisfaction with Breasts, Satisfaction with Outcome, Psychosocial Well-being, Sexual Well-being, Physical Well-being: Chest, and Physical Well-being: Abdomen. The raw scores of the BREAST-Q domains were converted to scores between 0 (worst) and 100 (best) using the Q-Score software.[27]

Statistical Analysis

Twenty-five patients did not report their highest completed education level; these missing answers were imputed using a single imputation method. A propensity-score weighting for multiple treatments was calculated according to the method of McCaffrey et al.[28] to adjust for covariates that predict receiving any one of the four surgical treatment options, thereby reducing the effects of confounding. The following clinical and sociodemographic characteristics were included in the propensity weight calculation: age at the time of survey, education, year of breast cancer diagnosis, year of surgery, chemotherapy, hormone therapy, and breast cancer recurrence. The EQ-5D Dutch general population reference sample was matched to all surgical groups using age and sex as the matching variables. Propensity weights were calculated by the Toolkit for Weighting and Analysis of Nonequivalent Groups Package for Stata (StataCorp, College Station, Texas).[29]

For all responding patients, propensity-adjusted patient and treatment characteristics and health-related quality of life were presented. Propensity weights were incorporated in the analyses using the Stata-SE14 survey (svy) postestimation function.[30] Mean scores, confidence intervals, and pairwise comparisons were subsequently obtained and performed using the margins regression estimation function. Column proportions were chi-square tested. The utilities resulting from the

EQ-5D per surgical treatment were stratified by experienced surgical complications. Utilities per surgical treatment were plotted over the course of time in 3-year intervals (≤3; 3 ≤ 6; 6 ≤ 9; >9), starting at the time of last breast reconstruction.

For statistical testing, two-sided values of $p \leq 0.05$ were considered statistically significant. All analyses were performed in Stata-SE14.[31]

RESULTS

A total of 1871 of 3804 patients (49 percent) responded, consisting of 615 breast-conserving surgery, 507 mastectomy, 330 autologous breast reconstruction, and 419 implant-based breast reconstruction patients. Table 1 presents patient and treatment characteristics. Nearly all autologous breast reconstruction procedures were abdominally based free-flap reconstructions. After propensity-weighted adjustment, estimated group sizes were reduced to 434.0 breast-conserving surgery, 386.3 mastectomy, 178.6 autologous breast reconstruction, and 295.5 implant-based breast reconstruction patients. Group sizes declined as patients with certain characteristics from one group occurred less frequently in another group, and thus received a relative score weight lower than 1. After propensity-weighted adjustment, balance was achieved for all variables, except for age and chemotherapy treatment.

Quality-of-Life Outcomes

Table 2 presents preference-based health-related quality-of-life outcomes at the time of survey per group. Unadjusted results for the outcomes presented Table 2 can be found in Supplemental Digital Content 1. [**See Table, Supplemental Digital Content 1**, which shows the mean patient-reported quality-of-life scores of 1871 breast cancer patients per surgical treatment and the Dutch general population, before (*left*) and after (*right*) propensity-weighted adjustment, ***http://links.lww.com/PRS/E97***.] After propensity-weighted adjustment, patients treated with mastectomy reported a statistically significant lower mean EQ-5D score (0.805) compared to all other surgical groups (breast-conserving surgery, 0.844; autologous breast reconstruction, 0.849; implant-based breast reconstruction, 0.850). Pairwise comparisons of the groups for the individual EQ-5D domains reflected these lower means for mastectomy as well (Fig. 1).

Furthermore, for two EORTC Quality of Life Questionnaire C30 functioning scales, statistically significant differences were found. First, patients treated with implant-based breast reconstruction reported a statistically significant higher mean physical functioning (87.97) than patients with breast-conserving surgery (84.53) or mastectomy (82.94), although the value was comparable to that reported for autologous breast reconstruction (85.62). Second, implant-based breast reconstruction patients reported a statistically significant higher mean role functioning (86.02) compared to patients treated with mastectomy (80.70). Within the symptom scales, statistically significant more favorable mean scores were found for breast-conserving surgery over mastectomy for pain (breast-conserving surgery, 15.41; mastectomy, 18.93) and financial problems (breast-conserving surgery, 5.23; mastectomy, 8.22).

Based on the EORTC Quality of Life Questionnaire BR23 scores, mean body image was significantly higher for breast-conserving surgery patients (breast-conserving surgery, 87.45; mastectomy, 80.49; autologous breast reconstruction, 82.28; implant-based breast reconstruction, 82.35). Breast-conserving surgery patients also reported the lowest mean arm symptoms (breast-conserving surgery, 12.68; mastectomy, 17.12; autologous breast reconstruction, 18.18; implant-based breast reconstruction, 16.82). In contrast, breast symptoms on average were more often reported by patients treated with breast-conserving surgery (13.45) than with mastectomy (9.94) or autologous breast reconstruction (8.79). Patients with autologous and implant-based breast reconstruction reported the highest mean sexual enjoyment (autologous breast reconstruction, 64.24; implant-based breast reconstruction, 63.80) compared to breast-conserving surgery or mastectomy (breast-conserving surgery, 57.03; mastectomy, 54.82).

For the BREAST-Q scales, patients with autologous breast reconstruction reported the highest mean Satisfaction with Breasts (autologous breast reconstruction, 71.29) compared to the other groups (breast-conserving surgery, 65.52; mastectomy, 60.65; implant-based breast reconstruction, 59.39). Interestingly, Satisfaction with Breasts for mastectomy and implant-based breast reconstruction did not differ significantly. Mean Satisfaction with Outcomes and Satisfaction with Nipples scores were significantly higher in autologous than in implant-based breast reconstruction patients (autologous breast reconstruction, 75.75; implant-based breast reconstruction, 66.37; and autologous breast reconstruction, 63.03; implant-based breast reconstruction, 54.96, respectively). Mastectomy patients reported the lowest mean Psychosocial Well-being (66.50) and Sexual Well-being (50.00).

Table 1. Patient-Reported Characteristics of 1871 Breast Cancer Patients per Surgical Treatment Group, before and after Propensity-Weighted Adjustment*

	Before Propensity-Weighted Adjustment				After Propensity-Weighted Adjustment			
	BCS	MAS	A-BR	I-BR	BCS	MAS	A-BR	I-BR
Group size, no.	615	507	330	419	434.0	386.3	178.6	295.5
Mean time variables ± SD, yr								
Age at the time of survey†‡	64.43 ± 9.07[a,b]	65.90 ± 10.67[a]	56.35 ± 9.17[b]	55.79 ± 10.44[b]	62.95 ± 9.67[a]	62.23 ± 10.37[a]	59.58 ± 9.72[b]	60.05 ± 9.96[b]
Time between MAS/BCS and survey†	6.14 ± 3.90[a]	7.28 ± 4.97[b]	7.87 ± 5.18[b]	7.65 ± 5.75[b]	7.04 ± 4.56[a]	6.86 ± 4.34[a]	6.61 ± 4.65[a]	7.04 ± 4.95[a]
Time between BR and survey†	N/A	N/A	5.67 ± 4.76[a]	6.20 ± 5.20[a]	N/A	N/A	4.93 ± 4.34[a]	5.75 ± 4.54[b]
Time between last BR surgery and survey	N/A	N/A	4.54 ± 4.34[a]	4.53 ± 3.67[a]	N/A	N/A	4.01 ± 3.78[a]	4.48 ± 3.32[a]
Treatment characteristics, %								
Reconstruction status§								
Unilateral BR	N/A	N/A	85.6	64.2	N/A	N/A	85.4	71.1
Bilateral BR	N/A	N/A	14.4	35.8	N/A	N/A	14.6	28.9
Previously had a BR	N/A	7.8	N/A	N/A	N/A	8.7	N/A	N/A
Never had BR and does not want BR	N/A	87.4	N/A	N/A	N/A	84.9	N/A	N/A
Never had BR but wants BR	N/A	4.6	N/A	N/A	N/A	6.4	N/A	N/A
Timing of reconstruction§								
Immediate BR	N/A	N/A	15.9	46.1	N/A	N/A	15.6	47.6
Delayed BR	N/A	N/A	83.0	53.5	N/A	N/A	82.6	52.0
Laterality of MAS								
Unilateral	N/A	85.6	87.9	67.1	N/A	86.1	89.9	74.4
Bilateral	N/A	14.4	12.1	32.9	N/A	13.9	10.2	25.6
Recurrence†								
No recurrence	93.8	85.8	90.9	89.3	90.1	91.0	91.4	90.9
Local recurrence	1.1	7.7	5.5	5.7	3.5	4.1	4.0	4.5
Distant recurrence	5.0	6.5	3.6	5.0	6.4	4.9	4.6	4.5
Patient-reported complications								
No complication	84.2	63.5	56.7	66.5	82.3	64.6	53.4	68.4
Complication	15.8	22.4	43.3	33.5	17.7	21.5	46.6	31.6
Unknown	0.0	14.1	0.0	0.0	0.0	13.9	N/A	N/A
No. of comorbidities								
No comorbidities	47.3	42.2	51.8	52.7	47.1	48.2	49.8	48.7
One	32.5	35.3	30.9	34.8	32.6	34.3	12.6	36.4
Two	14.5	16.6	12.4	8.1	15	13.2	32.9	9.4
Three or more	5.7	5.9	4.8	3.9	4.5	4.3	4.7	4.3
Treated with								
Chemotherapy†	24.2	44.2	63.9	48.4	37.4	42.7	47.6	43.9
Radiotherapy	94.3	36.9	35.8	24.1	94.9	33.0	30.6	22.6
Hormone therapy†								
Yes, still receiving treatment	19.0	24.7	29.1	24.1	58.2	56.3	57.2	58.8
Yes, completed	67.5	50.3	48.5	56.8	23.8	23.4	22.2	21.6
Patient characteristics, %								
Highest completed education†								
Lower level	24.9	28.8	18.2	14.6	24.0	23.4	21.5	18.1
Midlevel	55.1	48.1	56.1	55.8	54.5	53.6	52.7	55.3
High-level professional schooling	20.0	23.1	25.8	29.6	21.5	23.1	25.8	26.6
Employment status								
Employed outside home	30.7	23.5	54.8	58.0	35.3	31.6	45.6	45.6
Employed from home	1.8	5.7	7.9	4.1	1.6	5.1	10.17	3.6

(*Continued*)

Table 1. *Continued*

	Before Propensity-Weighted Adjustment				After Propensity-Weighted Adjustment			
	BCS	MAS	A-BR	I-BR	BCS	MAS	A-BR	I-BR
Not employed	52.8	59.6	33.0	32.2	49.0	52.4	37.1	42.8
Other	14.6	11.2	4.2	5.7	14.1	10.9	7.2	8.0
Household composition								
One-person household	19.3	22.7	17.6	15.0	17.9	18.8	22.7	19.9
Multiperson household	80.7	77.3	82.4	85.0	82.1	81.2	77.4	80.1
Relationship status								
Single	7.6	7.7	10.9	9.1	7.8	9.2	9.6	8.7
Married	77.9	74.2	77.3	78.3	79.0	76.6	73.5	76.6
Divorced	3.6	4.1	5.2	7.4	3.0	4.9	5.9	8.9
Widow	10.9	14.0	6.7	5.3	10.2	9.3	10.9	7.6
Children								
Yes	19.8	22.1	49.1	48.7	14.6	28.1	42.8	37.0
No	80.2	77.9	50.9	51.3	75.4	71.9	57.2	63.0

BCS, breast conserving surgery; MAS, mastectomy without breast reconstruction; BR, breast reconstruction; A-BR, mastectomy with autologous BR; I-BR, mastectomy with implant BR; GP, general population (The Netherlands reference cohort); N/A, not applicable.
*Values in the same row and subtable not sharing the same superscript letters (*a* and *b*) were significantly different at $p < 0.05$ using the adjusted Wald test. Cells with no superscript letters were not included in the test. Tests assume equal variances. SD values for propensity weighted groups are an estimate of the population standard deviation (sigma).
†Variables used for propensity weighting.
‡Mean ages for the general population cohort: 46.87 years and 58.48 years unadjusted and adjusted by propensity score, respectively.
§Does not add up to 100 percent because of missing answers.

Effect of Complications on EQ-5D Outcomes

A total of 96 of 615 breast-conserving surgery patients (16 percent), 112 of 507 mastectomy patients (22 percent), 138 of 330 autologous breast reconstruction patients (42 percent), and 140 of 419 implant-based breast reconstruction patients (33 percent) reported having experienced complications following surgery (unadjusted groups). After propensity-weighted adjustment, patients treated with either breast-conserving surgery, mastectomy, or autologous breast reconstruction who had experienced complications, showed statistically significant lower mean utilities than patients from the same groups who had not experienced complications (Table 3). Unadjusted results for the outcomes presented in Table 3 are shown in Supplemental Digital Content 2. [**See Table, Supplemental Digital Content 2**, which shows the mean EQ-5D-5L utilities for 1871 breast cancer patients with or without surgical complications per treatment group and the Dutch general population, before (*left*) and after (*right*) propensity-weighted adjustment, ***http://links.lww.com/PRS/E98***.] However, mastectomy patients without complications (0.818) reported means similar to autologous breast reconstruction patients with complications (0.816) and implant-based breast reconstruction patients with complications (0.861). Mean EQ-5D scores of mastectomy patients who previously had undergone a breast reconstruction (e.g., failed breast reconstruction) and who never had undergone a breast reconstruction did not differ significantly from each other ($p = 0.943$, results not shown).

For both breast reconstruction groups, problems reported according to the EQ-5D domain were stratified by complications (Fig. 2). Autologous breast reconstruction patients with complications reported problems for the usual activities and pain/discomfort domain statistically significant more often than autologous breast reconstruction patients without complications.

Figure 3 includes box plots presenting timelines of the utilities for autologous and implant-based breast reconstruction patients who had experienced complications, unadjusted by propensity weighting. In the first 3 years after a complicated breast reconstruction, a relatively large proportion of autologous breast reconstruction patients experienced a severe impact on health-related quality of life. This negative impact on health-related quality of life recovered with time for both treatment modalities. However, a larger proportion of implant-based breast reconstruction patients seemed to recover

Table 2. Mean Patient-Reported Quality-of-Life Scores of 1871 Breast Cancer Patients per Surgical Treatment and the Dutch General Population, after Propensity-Weighted Adjustment*

	BCS (95% CI)	MAS (95% CI)	A-BR (95% CI)	I-BR (95% CI)	GP (95% CI)
Group size, no.	434.0	386.3	178.6	295.5	N/A
EQ-5D-5L					
Utilities	0.844[a] (0.829–0.859)	0.805[b] (0.787–0.823)	0.849[a] (0.828–0.871)	0.850[a] (0.823–0.877)	0.833[a] (0.812–0.854)
VAS Score	77.76[a] (76.02–79.51)	76.48[a] (74.75–78.22)	79.24[a] (76.76–81.72)	77.58[a] (75.52–79–65)	78.88[a] (77.08–80.69)
EORTC-QLQ-C30					
Global Health Status	80.00[a] (78.26–81.75)	79.01[a] (77.14–80.87)	81.38[a] (79.22–83.54)	80.16[a] (78.07–82.25)	N/A
Function scales					
Physical function	84.53[a] (83.02–86.04)	82.94[a] (81.32–84.55)	85.62[ab] (83.30–87.85)	87.97[b] (85.63–90.31)	N/A
Role function	84.35[a] (82.34–86.36)	80.70[b] (80.84–87.19)	84.02[ab] (82.82–89.22)	86.02[a] (82.82–89.22)	N/A
Emotional function	85.36[a] (83.36–87.18)	83.84[a] (81.90–85.78)	87.00[a] (84.47–89.51)	85.04[a] (82.40–87.67)	N/A
Cognitive function	84.14[a] (82.21–86.06)	84.32[a] (82.32–86.31)	83.67[a] (80.53–86.82)	84.97[a] (82.29–87.65)	N/A
Social function	88.82[a] (87.01–90.63)	86.94[a] (87.01–90.63)	88.02[a] (85.54–90.50)	87.48[a] (84.40–90.55)	N/A
Symptom scales					
Fatigue	21.82[a] (19.77–23.87)	22.54[a] (20.30–24.77)	22.39[a] (19.27–25.51)	20.21[a] (17.47–22.94)	N/A
Nausea and vomiting	2.72[a] (1.98–3.46)	3.31[a] (2.25–4.38)	2.83[a] (1.76–3.90)	3.35[a] (1.40–5.30)	N/A
Pain	15.41[a] (13.56–17.25)	18.93[b] (16.53–21.32)	17.18[ab] (14.07–20.28)	15.89[ab] (12.87–18.90)	N/A
Dyspnea	14.28[a] (12.18–16.39)	12.22[a] (10.12–14.31)	13.39[a] (9.75–17.03)	10.82[a] (8.06–13.59)	N/A
Insomnia	22.76[a] (20.09–25.44)	22.69[a] (19.93–25.44)	20.37[a] (16.87–23.87)	25.11[a] (21.10–29.11)	N/A
Appetite loss	5.87[a] (4.45–7.30)	4.08[a] (2.90–5.26)	3.81[a] (2.25–5.37)	3.90[a] (1.78–6.03)	N/A
Constipation	6.98[a] (5.38–8.59)	7.07[a] (5.34–8.79)	7.96[a] (5.29–10.63)	5.29[a] (3.80–6.78)	N/A
Diarrhea	4.81[a] (3.52–6.10)	4.43[a] (3.14–5.72)	3.24[a] (1.96–4.51)	4.65[a] (3.11–6.19)	N/A
Financial problems	5.23[a] (3.77–6.69)	8.22[b] (6.16–10.28)	12.30[b] (8.41–16.19)	7.71[ab] (5.21–10.22)	N/A
EORTC-QLQ-BR23					
Function scales					
Body image	87.45[a] (85.45–89.45)	80.49[b] (78.24–82.74)	82.28[b] (79.01–85.55)	82.35[b] (79.83–84.88)	N/A
Sexual functioning	27.90[a] (25.23–30.58)	27.51[a] (24.80–30.22)	31.95[ab] (28.02–35.89)	33.35[b] (29.99–36.72)	N/A
Sexual enjoyment	57.03[a] (53.03–61.02)	54.82[a] (51.07–58.57)	64.24[b] (59.27–69.21)	63.80[b] (60.06–67.54)	N/A
Future perspective	74.51[a] (72.17–76.85)	71.93[a] (69.15–74.71)	76.14[a] (72.34–79.95)	75.03[a] (72.21–77.85)	N/A
Symptom scales					
Systemic therapy side-effects	12.60[a] (11.57–13.64)	12.74[a] (11.49–13.99)	14.41[a] (12.41–16.40)	13.79[a] (12.08–15.50)	N/A
Breast symptoms	13.45[a] (11.80–15.11)	9.94[b] (8.60–11.28)	8.79[b] (6.88–10.71)	10.82[ab] (8.36–13.27)	N/A
Arm symptoms	12.68[a] (11.02–14.34)	17.12[b] (15.12–19.12)	18.18[b] (14.94–21.41)	16.82[b] (13.60–20.03)	N/A
Hair loss	4.25[a] (2.78–5.71)	4.86[a] (3.37–6.35)	6.50[a] (4.02–8.98)	5.47[a] (3.58–7.37)	N/A
BREAST-Q					
Satisfaction with Breasts	65.52[a] (63.43–67.61)	60.65[b] (58.79–62.51)	71.29[c] (68.66–73.92)	59.39[b] (57.18–61.60)	N/A
Satisfaction with Outcome	N/A	N/A	75.75[a] (72.52–78.99)	66.37[b] (63.66–69.08)	N/A
Psychosocial Well-being	73.77[a] (71.70–75.83)	66.50[b] (64.68–68.32)	75.78[ac] (72.94–78.63)	71.60[a] (69.30–73.90)	N/A
Sexual Well-being	62.70[a] (59.92–65.48)	50.00[b] (47.44–52.55)	63.33[a] (58.91–67.75)	56.38[c] (52.88–59.88)	N/A
Physical Well-being: Chest	67.39[a] (65.17–69.61)	73.47[b] (71.78–75.16)	75.81[bc] (73.56–78.06)	72.64[b] (70.61–74.66)	N/A
Physical Well-being: Abdomen	N/A	N/A	75.81 (73.56–78.06)	N/A	N/A
Satisfaction Nipple			63.03[a] (58.82–67.25)	54.96[b] (49.38–60.54)	N/A

BCS, breast conserving surgery; MAS, mastectomy without breast reconstruction; A-BR, mastectomy with autologous breast reconstruction; I-BR, mastectomy with implant breast reconstruction; GP, general population; N/A, not applicable; EORTC, European Organization for Research and Treatment of Cancer; QLQ, Quality of Life Questionnaire; VAS, visual analogue scale.
*Values in the same row and subtable not sharing the same superscript letters (*a*, *b*, and *c*) were significantly different at $p < 0.05$ using the adjusted Wald test. Cells with no superscript letters were not included in the test. Tests assume equal variances.

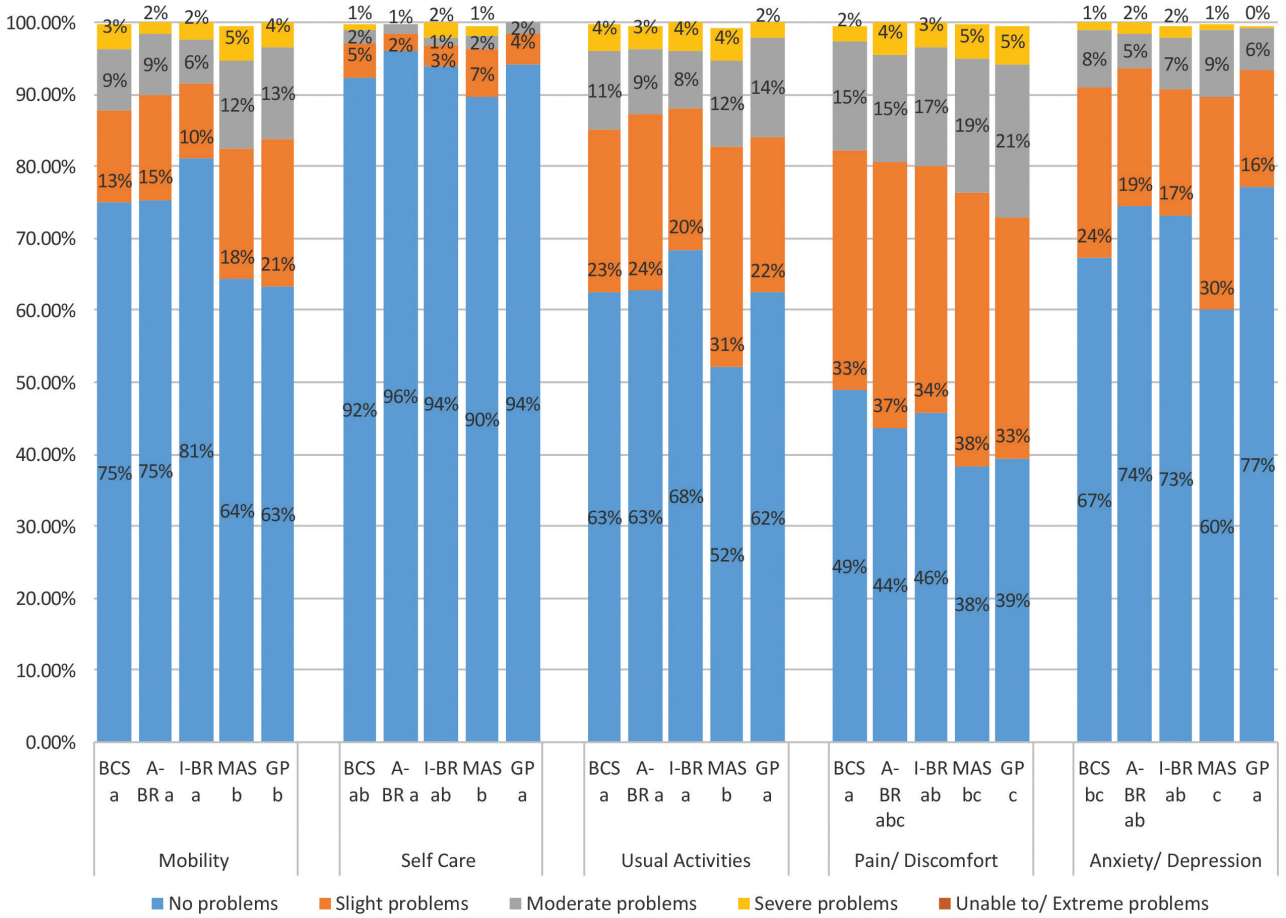

Fig. 1. Propensity-weighted EQ-5D-5L subscale per surgical treatment and weighted Dutch general population. *BCS*, breast-conserving surgery; *MAS*, mastectomy without breast reconstruction; *A-BR*, mastectomy with autologous breast reconstruction; *I-BR*, mastectomy with implant breast reconstruction; *GP*, general population. Values in the same domain not sharing the same letter (*a*, *b*, and *c*) were significantly different at $p < 0.05$ using the adjusted Wald test.

up to the degree that they did not report problems on any of the EQ-5D dimensions within 6 to 9 years after the last breast reconstruction surgery, compared to a much smaller portion of autologous breast reconstruction patients.

DISCUSSION

This study aimed to compare health-related quality-of-life outcomes for four common surgical breast cancer treatment options (breast-conserving surgery, mastectomy, autologous breast reconstruction, and implant-based breast reconstruction) to improve the evidence and consequently decision-making about breast cancer surgery. We found that mastectomy patients reported the lowest mean health-related quality of life (EQ-5D) and functioning (EORTC Quality of Life Questionnaire C30). Based on the BREAST-Q, autologous breast reconstruction patients had statistically significant higher Satisfaction with Outcome and Satisfaction with Breasts and Sexual Well-being scores than implant-based breast reconstruction patients. Patients with complications (except for implant-based breast reconstruction) reported statistically significant lower health-related quality of life (EQ-5D) than patients without complications; complications in autologous breast reconstruction patients resulted in a substantially lower health-related quality of life than in implant-based breast reconstruction patients.

The results show the added value of breast conservation and reconstruction compared to mastectomy; however, the differences between breast-conserving surgery, implant-based breast reconstruction, and autologous breast reconstruction were subtle. Indeed, we found many statistically significant differences, but given the high statistical power of our large study, most of them were small. Thus, on average, we found few clinically relevant differences between breast-conserving surgery, implant-based breast reconstruction,

Table 3. Mean EQ-5D-5L Utilities for 1871 Breast Cancer Patients with or without Surgical Complications per Treatment Group and the Dutch General Population after Propensity-Weighted Adjustment*

	BCS (95% CI)	MAS (95% CI)	A-BR (95% CI)	I-BR (95% CI)	GP (95% CI)
Group size, no.	434.0	386.3	178.6	295.5	N/A
No complications, %	82.3	75.0	53.4	68.4	100
Mean EQ-5D-5L utilities	0.859[a] (0.844–0.875)	0.818[b] (0.796–0.840)	0.878[a] (0.854–0.902)	0.847[ab] (0.810–0.884)	0.833[b] (0.812–0.854)
Complications, %	17.7	25.0	46.6	31.6	
Mean EQ-5D-5L utilities	0.771[a] (0.729–0.812)	0.771[a] (0.736–0.806)	0.816[ab] (0.780–0.853)	0.861[b] (0.834–0.888)	N/A

BCS, breast-conserving surgery; MAS, mastectomy without breast reconstruction; BR, breast reconstruction; A-BR, mastectomy with autologous BR; I-BR, mastectomy with implant BR; GP, general population; N/A, not applicable.
*Values in the same row and subtable not sharing the same superscript letters (*a* and *b*) were significantly different at $p < 0.05$ using the adjusted Wald test. Cells with no superscript letters were not included in the test. Tests assume equal variances.

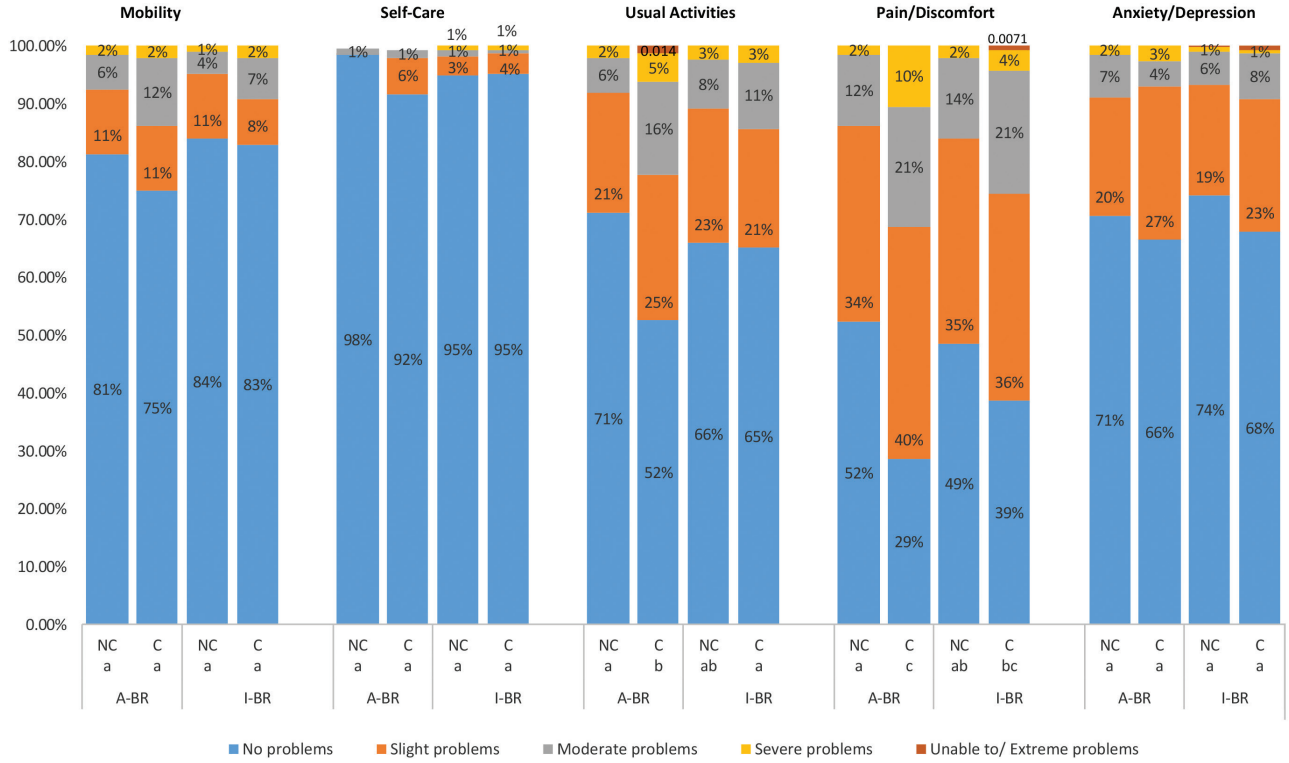

Fig. 2. EQ-5D-5L subscale contrasting autologous breast reconstruction and implant-based breast reconstruction with or without surgical complication (unadjusted for propensity score). *A-BR*, mastectomy with autologous breast reconstruction; *I-BR*, mastectomy with implant breast reconstruction; *GP*, general population; *C*, surgical complications; *NC*, no surgical complications. Values in the same domain not sharing the same letter (*a*, *b*, and *c*) were significantly different at $p < 0.05$ using the adjusted Wald test. Cells without letters (*a*, *b*, or *c*) were not included in the test. Tests assume equal variances.

and autologous breast reconstruction for the various health-related quality-of-life domains. However, the benefits of these subtle differences over a long time are a good reason to consider them in clinical decision-making, specifically when considering the effects of complications and the patient's attitude toward the risks of complications.

Only one other study that reported utilities for surgically treated breast cancer patients receiving breast reconstruction was found (immediate implant-based breast reconstruction patients; mean score, 0.83).[14] We found lower mean health-related quality-of-life scores reported by mastectomy patients and benefits in some health-related quality-of-life domains for breast-conserving surgery patients (higher body image and more favorable arm symptom) over all other surgically treated groups, which confirms previously reported results.[15,20,32] The benefits of autologous compared to implant-based breast reconstruction (higher mean Satisfaction with Breasts/Satisfaction with Outcome/Satisfaction with Nipples, and

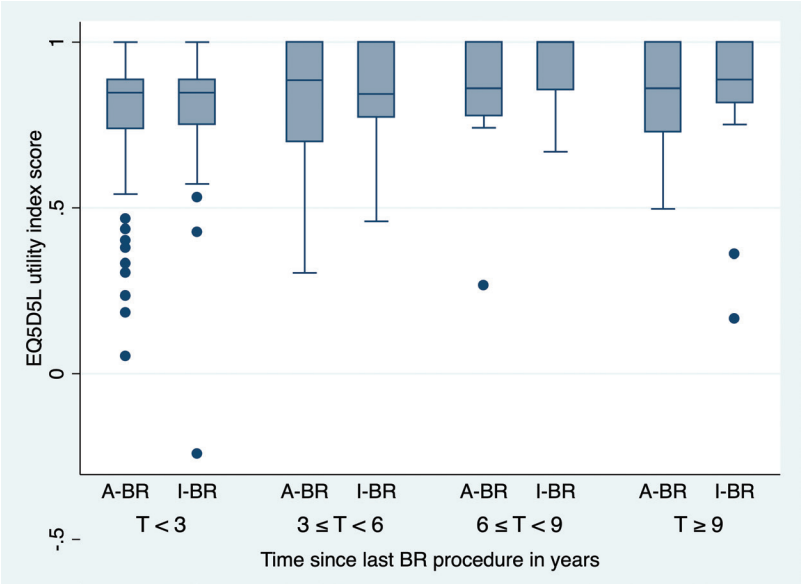

Fig. 3. EQ-5D-5L utilities over time in years (time between last breast reconstruction and questionnaire) for breast cancer patients following breast reconstruction with complications. *A-BR*, mastectomy with autologous breast reconstruction; *I-BR*, mastectomy with implant breast reconstruction.

Sexual Well-being) were also reported by Santosa et al.[22] However, in contrast, both the present study and Thorarinsson et al.[33] did not find statistically significant differences between autologous and implant-based breast reconstruction on either the EQ-5D-5L or the EORTC Quality of Life Questionnaire outcomes. Thus, although the BREAST-Q results suggest that the patient's perception of their reconstructed breast(s) is favorable for autologous over implant-based breast reconstruction, this does not necessarily lead to better outcomes in terms of overall health-related quality of life.

The second aim was to assess the impact of complications after different surgical treatments. Indeed, if any clinically relevant differences were found,[34] they seemed to be related to complications. Specifically for autologous breast reconstruction, one should not ignore the impact of complications.[35] Autologous breast reconstruction patients with complications (versus those without complications) had statistically significant lower mean utilities as measured with the EQ-5D, and more often had problems in the usual activities and pain/discomfort domains. Also, mean scores recovered faster for implant-based breast reconstruction patients than for autologous breast reconstruction patients. Finally, a larger proportion of autologous breast reconstruction patients never recovered up to the degree that they did not report problems on any of the EQ-5D dimensions.

The faster recovery after complications of implant-based breast reconstruction patients could explain why the utilities in patients with and without complications did not differ statistically. The symptoms and the longer lasting impact of complications in autologous breast reconstruction patients may be inherent in the type of complications associated with these procedures. More specifically, failure of an implant-based breast reconstruction is often attributable to an infection, resulting in removal of the implant, later often followed by a new implant-based breast reconstruction. Total flap failure following autologous breast reconstruction requires a new and additional donor site, with its own donor-site issues and complication risks. Women experience breast reconstruction (flap) failure as an emotionally very difficult life event,[36] although previous studies have shown that physical and mental health after a breast reconstruction complication generally recover to normal levels after a period.[37,38]

By measuring health-related quality of life using multiple, validated patient-reported outcome measures in a large sample of patients following different types of breast cancer surgery, we were able to improve earlier, smaller, and less consistent attempts to assess health-related quality of life in surgically treated breast cancer patients. Our statistically significant results confirm the findings of studies mentioned previously,[15,20,22,32,35] thereby

supporting the added value of breast conservation and reconstruction for breast cancer patients.

Furthermore, no predominant treatment option was found. This stresses the idea that all treatment options (that are physically feasible) should be considered for every patient. The ultimate treatment decision should be predominantly based on the patient's preferences, resulting in the alignment of the favorable assets (or domain scores) of each procedure and the patient's goals and expectations with the expected final result of each procedure in addition to their attitudes toward complication risks. Although we have investigated decision-making in a previous study in a similar cohort of patients,[39] it would have been interesting to have insight in the treatment rationale for the current patient cohort.

This study demonstrates the use of the unique assets of the EQ-5D, a "preference-based," standardized generic measure of health status that is suitable for a wide comparison of treatment options.[40,41] A benefit of this preference-based health-related quality-of-life measure compared to commonly applied "non–preference-based" measures such as the EORTC instrument and the BREAST-Q is that its outcomes can be aggregated over time and, after multiplication with survival time, provides quality-adjusted life-years.[41] The EQ-5D utilities can be related to the period of each health state, and can therefore combine the "utility" of the advantages and disadvantages, such as complications of surgical procedures. Note that our data were not able to fully solve the question of how the utility of the benefits of a surgical procedure relates to the disutility of complications, as this requires longitudinal data to represent the EQ-5D values and the time lived with or without a given complication. Nevertheless, the present data can still provide insights in the tradeoff between benefits and complications of the different surgical procedures.

Of further importance is that previous studies have not yet described utilities for the complete range of breast cancer surgery options. This currently complicates the implementation of health economics and reimbursement decision-making. Clinical treatment value should be related to health care costs, which is the ultimate goal toward creating value-based health care.[42] In our subsequent study, we will relate costs to the outcomes we found in the present study.

Some limitations are relevant in the interpretation of our results. First, although propensity-weighted adjustment was used to minimize the effects of bias caused by including patients from an observational cohort, one cannot exclude that relevant variables may still have influenced the results of our study.[28] For instance, surgical treatment selection might be based on severity of comorbidities or performance status, which were both not available in our data. Nonresponse bias could have been induced by socioeconomic and procedure-related differences, as described by Berlin et al.[43] Besides, surveys introduce a certain arbitrariness, as patients might understand or interpret questions or experiences in unintended ways.

CONCLUSIONS

We conclude that health-related quality of life of mastectomy patients was often the lowest, supporting the added value of breast conservation and reconstruction in breast cancer patients. Furthermore, we found that each surgical procedure has subtle favorable assets, with the most notable related to complications: a complication in autologous breast reconstruction patients resulted in a substantially lower health-related quality of life than in implant-based breast reconstruction patients, and mastectomy patients without complications had similar or lower mean EQ-5D scores compared to autologous or implant-based breast reconstruction patients with complications. This could support a discussion about the alignment of the patient's goals, expectations, and attitudes toward complication risks with the expected final result of each procedure.

Casimir A. E. Kouwenberg, M.D., M.Sc.
Department of Plastic and Reconstructive Surgery
Erasmus MC Cancer Institute
University Medical Centre Rotterdam
P.O. Box 2040
Rotterdam 3000 CA, The Netherlands
kouwenberg@gmail.com

ACKNOWLEDGMENTS

The authors thank all women who participated in this study. The data that support the findings of this study are not publicly available. Data are available from the authors upon reasonable request. The study was not preregistered in an independent, institutional registry.

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