Clinical Pain Research

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Breast reconstruction after breast cancer surgery – persistent pain and quality of life 1–8 years after breast reconstruction

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Abstract

reconstructions with special focus on chronic postsurgical pain (CPSP) in a larger cohort of breast cancer survivors. Methods: A cross-sectional study on 121 women with mastectomy and breast reconstruction after mean 2 years 4 months follow up. The mean time from breast reconstruction to the follow-up visit was 4 years 2 months. We studied surveys on pain (Brief Pain Inventory, BPI and Douleur Neuropathique 4, DN4), quality of life (RAND-36 health survey), sleep (insomnia severity questionnaire, ISI), mood (Beck's Depression Index, BDI; Hospital Anxiety and Depression Scale, HADS), and a detailed clinical sensory status. Patients were divided into three groups: abdominal flap (Deep inferior epigastric perforator flap, DIEP; Free transverse rectus abdominis flap, fTRAM, and Pedicled transverse rectus abdominis flap, pTRAM), dorsal flap (Latissimus dorsi flap, LD and Thoracodorsal artery perforator flap, TDAP), and other (Transverse myocutaneous gracilis flap, TMG; implant). Clinically meaningful pain was defined $\geq 4/10$ on a numeric rating scale (NRS).

Objectives: To assess the long-term outcome of breast

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Eija Kalso, Department of Anaesthesiology, Intensive Care and Pain Medicine, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

Tuomo Meretoja, Breast Surgery Unit, Comprehensive Cancer Center, University of Helsinki and Helsinki University Hospital, Helsinki, Finland We used patients' pain drawings to localize the pain. We assessed preoperative pain NRS from previous data.

Results: 106 (87.6%) of the patients did not have clinically meaningful persistent pain. We found no statistically significant difference between different reconstruction types with regards to persistent pain (p=0.40), mood (BDI-II, p=0.41 and HADS A, p=0.54) or sleep (p=0.14), respectively. Preoperative pain prior to breast reconstruction surgery correlated strongly with moderate or severe CPSP. **Conclusions:** Moderate to severe CPSP intensity was present in 14% of patients. We found no significant difference in the prevalence of pain across different reconstruction types. Preoperative pain associated significantly with postoperative persistent pain.

Keywords: affect; diagnostic tests; mammaplasty; mastectomy; pain; pain measurement.

Introduction

Aesthetic outcomes of mastectomy are often considered unsatisfactory and stigmatizing, which have led to adverse social and psychological effects for women undergoing mastectomy [1, 2]. Consistent with this, women with successful breast reconstruction have shown higher quality of life compared with women with mere mastectomy [3–5]. With increasing cancer survival rates, about 40% of women choose breast reconstruction after mastectomy [6]. The American Society of Plastic Surgeons estimates that a total of 107,238 breast reconstructions were performed in the United States in 2019 [7].

There are multiple breast reconstruction options from implants to various autologous tissue reconstruction types. In recent years, autologous tissue reconstructions have become more prevalent as they have shown higher patient reported satisfaction [8–12].

Acute complications for breast reconstruction include total or partial flap loss, donor site morbidity, skin necrosis, infection, seroma, and venous thromboembolism [13].

The risk of complications grows with age and increased body mass index (BMI) [14]. There is limited knowledge of the long-term side effects of breast reconstructions such as persistent pain of the surgical area. Recent studies have found no difference between breast reconstruction and mastectomy alone in the development of chronic postoperative pain [15–17].

We studied those patients from a larger breast cancer survivors' study [18] who later had breast reconstruction surgery. We aimed to characterize the outcomes between different breast reconstructions and to study whether persistent pain, sensory findings, quality of life, sleep, or mood differed in patients depending on the type of breast reconstruction.

Patients and methods

Patients

The present cohort is part of an earlier study of 1,000 women operated for breast cancer, where the preoperative pain NRS was assessed [18]. Of these 1,000 patients, 402 attended a follow up visit four to nine years after the index breast cancer operation [19]. There, patients filled in questionnaires about demographics, pain in the operated area and elsewhere, mood, sleep, and quality of life. A neurologist performed a detailed clinical sensory examination of the upper body. Patients with breast reconstruction were eligible for the present study.

Pain and sensory assessment

At the follow-up visit, patients drew the possible pain location in a patient body map. We used Brief Pain Inventory (BPI) to assess pain NRS of the operative area and/or elsewhere [20]. We considered numeric rating scale (NRS) ≥ 4/10 as clinically meaningful pain (0 meaning no pain and 10 the worst imaginable pain). To study possible neuropathic features in the persistent postsurgical pain, we used the Douleur Neuropathique 4 questionnaire (DN4) [21]. A score ≥ 4/10 indicates likely neuropathic pain.

To classify neuropathic pain, a sensory examination of the pain area is essential [22]. Here, the same neurologist (HH) performed a detailed sensory examination of the upper body including light touch by cotton wool, static allodynia by finger compression, dynamic allodynia by painter's brush, pinprick sensation by a cocktail stick, and cold and warm sensation by a metal roller. The sensory findings were drawn to a patient body map. If any of these sensory tests caused pain, it was classified as evoked pain and NRS of the pain intensity was

Patients were graded according to the latest neuropathic pain (NP) grading system to possible or probable and definite postsurgical NP [22]. There, sensory changes and pain location are in the same plausible area. In addition to these, to reach a definite NP criterion in this cohort, a surgeon-verified nerve resection of the ICBN was required.

We evaluated the impact of preoperative pain at the operative area for the chronic postoperative pain by recording pain NRS nearby before the reconstruction procedure. These data were obtained from the previous larger cohort [18], where we had data of the individual preoperative pain intensity of the operative area in NRS. After index surgery, the postoperative pain was followed at one month, three months, six months, one year, and yearly up to five years [18]. If the reconstruction was performed within one month after index surgery, we used the preoperative NRS of index surgery.

Mood, sleep, and quality of life questionnaires

For mood and sleep measures, we used Beck Depression Inventory II (BDI) (scores from 0 to 63 and scores from 10 to 18 indicate mild, 19 to 29 moderate, and ≥30 severe depression) [23], Hospital Anxiety and Depression Scale (HADS) (HADS-A (anxiety) and HADS-D (depression) both score from 0 to 21 with score 8 to 10 with mild symptoms and score ≥11 indicates clinically meaningful symptoms) [24], Pain Catastrophizing Scale (PCS) (scores from 0 to 52 and score ≥30 indicate clinically meaningful pain catastrophizing) [25], and the Insomnia Severity Index (ISI) (scores from 0 to 28 with score 8 to 14 indicating mild insomnia, score 15 to 21 moderate insomnia, and score ≥22 clinically severe insomnia) [26]. Quality of life was studied by RAND-36 questionnaire [27].

Statistical analysis

For testing distributions of normality, we used the Kolmogorov-Smirnov test and the Shapiro-Wilk test. For non-normally distributed and categorical variables we used Mann-Whitney U-test for and χ^2 tests. For finding differences between the studied groups we used the Kruskal-Wallis test. For correlations we used Pearsons r.

Average pain NRS from the BPI questionnaire and evoked pain NRS in the clinical examination were divided into separate categories and the type of reconstruction was also controlled. Reconstruction types were categorized into abdominal flaps (DIEP and TRAM), dorsal flaps (LD and TDAP) and other reconstruction types (Implant, TMG and Fat Grafting). The patient pain drawings were scanned and digitalized. From these drawings we constructed a heatmap of pain prevalence based on how many different patients had reported pain in a given area.

We measured variables for age, BMI, depression (yes/no, cutoff≥19 in BDI and ≥11 in HADS-D), anxiety (yes/no, cut-off≥11 in HADS-A), and quality of life (RAND-36).

Two-tailed $p \le 0.05$ was considered statistically significant. Statistical analyses were performed using SPSS 22.0 version for Windows (SPSS Inc., Chicago, IL, USA).

Results

Patients

Of the 402 patients, 121 with breast reconstruction were eligible for the present study (Figure 1). Of the 121 patients,

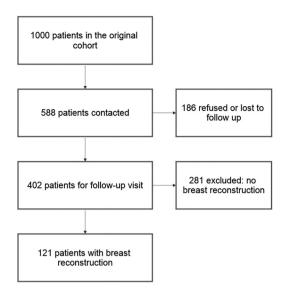


Figure 1: Patient selection flowchart.

106 (87.6%) had delayed and 15 (12.4%) an immediate breast reconstruction.

The demographics of the patients are presented in Table 1. The mean time from mastectomy to breast reconstruction was two years four months. The mean time from breast reconstruction to the followup visit was four years two months. Majority of the patients had never smoked and

used alcohol only moderately. Most patients were highly educated and married.

Most of the patients had either Grade II or III ductal or lobular breast cancer at the time of diagnosis and they had undergone mastectomy with either axillary lymph node dissection or sentinel lymph node biopsy prior to breast reconstruction (Table 2). 106 (87.6%) patients had received varying adjuvant breast cancer treatments: chemotherapy 88 (72.7%), radiotherapy 44 (36.4%), and endocrine therapy 80 patients (66.1%). The perioperative status of the intercostobrachial nerve (ICBN) as reported by the surgeon are shown in Table 2.

Breast reconstruction types

Of the 121 patients with breast reconstruction, most common reconstructions were autologous tissue reconstructions with latissimus dorsi (LD) and deep inferior epigastric artery perforator (DIEP) flaps (Table 3). The timing of reconstruction was immediate for 15 (12.4%) and delayed for 106 (87.6%) patients. 23 (19.1%) patients needed at least one additional fat grafting to enhance the reconstructed breast. 22 (18.2%) patients needed reoperation due to complications. Most of these were surgical revisions or evacuation of hematoma (Table 3). 59 (48.8%) patients also had plastic

Table 1: Patients characteristics.

	Abdominal flap	Dorsal flap	Other	All
Age, mean (SD), years	55.8 (7.2)	58.8 (7.4)	54.5 (9.8)	56.9 (7.9)
Time from mastectomy, mean (SD), months	80.8 (14.5)	79.5 (16.5)	77.6 (13.1)	79.6 (15.1)
Time from reconstruction, mean (SD), months	47.4 (20.7)	56.2 (22.8)	43.1 (19.9)	50.6 (22.0)
BMI, mean, SD	26.1 (2.9)	25.0 (3.6)	23.0 (3.7)	25.0(3.5)
Marital status, number, %				
Married or cohabitating	30 (66.7)	28 (51.9)	8 (36.4)	66 (54.5)
Single	7 (15.6)	10 (18.5)	6 (27.3)	23 (19.0)
Divorced or widowed	8 (17.8)	16 (29.6)	8 (36.4)	32 (26.4)
Education level, number, %				
Low	1 (2.2)	6 (11.1)	0 (0.0)	7 (5.8)
Moderate	8 (17.8)	16 (29.6)	2 (9.1)	26 (21.5)
High	36 (80.0)	32 (59.3)	20 (90.9)	88 (72.7)
Smoking, number, %				
Smoker	8 (17.8)	9 (16.7)	1 (4.5)	18 (14.9)
Ex-smoker	14 (31.1)	16 (29.6)	10 (45.5)	40 (33.1)
Never smoked	23 (51.1)	29 (53.7)	11 (50.0)	63 (52.1)
Alcohol consumption, number, %				
Abstinent	3 (6.7)	8 (14.8)	2 (9.1)	13 (10.7)
<6 doses	33 (73.3)	38 (70.4)	18 (81.8)	89 (73.6)
≥6 doses	9 (20.0)	8 (14.8)	2 (9.1)	19 (15.7)

Table 2: Breast cancer type and treatment.

	Abdominal flap	Dorsal flap	Other	All
Histology of tumor, number, %				
In situ	2 (4.4)	4 (7.4)	1 (4.5)	7 (5.8)
Ductal	28 (62.2)	31 (57.4)	15 (68.2)	74 (61.2)
Lobular	8 (17.8)	14 (25.9)	3 (13.6)	25 (20.7)
Other	7 (15.6)	5 (9.3)	3 (13.6)	15 (12.4)
Tumor grade, number, %				
I	6 (13.3)	14 (26.9)	6 (27.3)	26 (21.8)
II	14 (31.1)	25 (48.1)	6 (27.3)	45 (37.8)
III	25 (55.6)	13 (25.0)	10 (45.5)	48 (40.3)
Axillary surgery, number, %				
SNB	12 (26.7)	28 (51.9)	6 (27.3)	46 (38.0)
Axillary lymph node dissection	33 (73.3)	26 (48.1)	16 (72.7)	75 (62.0)
ICBN resection, number, %				
Saved	9 (20.0)	25 (46.3)	6 (27.3)	40 (33.1)
Partially saved	20 (44.4)	20 (37.0)	15 (68.2)	55 (45.5)
Resected	12 (26.7)	6 (11.1)	0 (0.0)	18 (14.9)
Not determined	4 (8.9)	3 (5.6)	1 (4.5)	8 (6.6)
Chemotherapy, number, %	40 (88.9)	32 (59.3)	16 (72.7)	88 (72.7)
Radiotherapy, number, %	21 (46.7)	13 (24.1)	10 (45.5)	44 (36.4)
Endocrine therapy, number, %	32 (71.1)	36 (66.7)	12 (54.5)	80 (66.1)
Diameter of tumor, median (IQR), mm	21 (16)	16 (13)	20 (14)	20 (13)
Number of lymph nodes removed, median (IQR)	19 (20)	8 (19)	16 (23)	16 (20)
Number of metastatic lymph nodes, median (IQR)	1 (3)	0 (1)	1 (3)	1 (2)

 Table 3: Breast reconstruction characteristics.

	Abdominal flap	Dorsal flap	Other	All
Reconstruction type, number, %				
DIEP	34 (75.6)			34 (28.1)
pTRAM	1 (2.2)			1 (0.8)
fTRAM	10 (22.2)			10 (8.3)
LD		53 (98.1)		53 (43.8)
TAP		1 (19)		1 (0.8)
TMG			6 (27.3)	6 (5.0)
Fat grafting			6 (27.3)	6 (5.0)
Silicone implants			10 (45.5)	10 (8.3)
Timing of reconstruction, number, %				
Immediate	4 (8.9)	11 (20.4)	0 (0.0)	15 (12.4)
Delayed	41 (91.1)	43 (79.6)	22 (100.0)	106 (87.6)
Unilateral or bilateral reconstruction, number, 9	%			
Unilateral	45 (100.0)	53 (98.1)	18 (81.8)	116 (95.9)
Bilateral	0 (0.0)	1 (1-9)	3 (13.6)	4 (3.3)
Reoperations due to complications, number, %				
No	37 (82.2)	42 (77.8)	20 (90.9)	99 (81.8)
Evacuation of hematoma	3 (6.7)	3 (5.6)	1 (4.5)	7 (5.8)
Revision	3 (6.7)	3 (5.6)	1 (4-5)	7 (5.8)
Other	2 (4.4)	6 (11.1)	0 (0.0)	8 (6.6)
Plastic surgery to the other side, number, %				
No	25 (55.6)	29 (53.7)	8 (36.4)	62 (51.2)
Reduction mammoplasty	20 (44.4)	25 (46.3)	9 (40.9)	54 (44.6)
Other	0 (0.0)	0 (0.0)	5 (22.7)	5 (4.1)
Abdominal-dorsal subgroup, number, %	45 (100.0)	54 (100.0)	22 (100.0)	121 (100.0)

surgery to the other breast, of which most (N = 54) were reduction mammoplasties (Table 3).

Chronic postsurgical pain

According to the neuropathic pain grading system, 41 patients (33.9%) had definite, 27 (22.3%) probable, and 7 (5.8%) possible chronic postsurgical NP (CPSNP). Featuring neuropathic pain component, 49 (40.5%) patients scored over 4 at the DN4 questionnaire.

Of the 121 patients, 17 (13.0%) had moderate or severe pain intensity (NRS \geq 4/10) and 43 (35.5%) presented mild pain (NRS from 1 to 3/10).

We found no significant difference in the prevalence of CPSNP between different reconstruction types. Due to the small sample size we combined DIEP and TRAM reconstructions into one group (N = 45) and compared them with LD reconstructions (N = 54). There were no statistically significant differences between the groups in the prevalence of persistent pain, worst evoked pain, or in DN4.

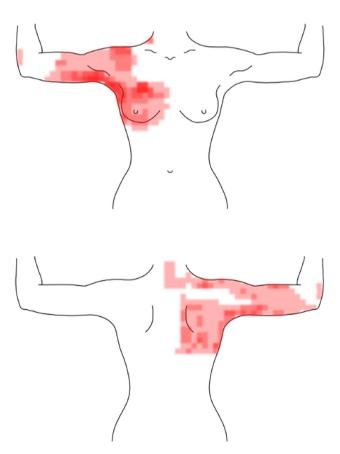


Figure 2: Pain heatmap based on patient drawn body maps. The darker the color, the more patients reported pain on the area. This map only includes patients who reported pain intensity of 4 or above in the NRS.

The most common pain areas after breast reconstruction according to patient pain drawings are illustrated in Figure 2.

Preoperative pain was significantly associated with CPSNP (correlation coefficient = 0.43, p<0.001)

Both radiotherapy and chemotherapy increased the incidence for evoked pain (p=0.039 and p=0.026, respectively), but not self-reported pain.

Sensory examination

In sensory examination, all patients perfomed sensory loss in some sensory modality. Forty-five (37.2%) patients (data missing for four patients) reported allodynia in clinical examination. All of the 45 patients had static mechanical allodynia for finger compression, two presented allodynia for light touch, seven for pinprick, one for cold sensation, and one had dynamic mechanical allodynia (painter's brush). Twenty (16.5%) patients reported evoked pain NRS 4 or more.

Psychological variables and quality of life

In general, the patients presented with no depression (BDI-II median 6.0), with 85 (70.2%) patients scoring lower than 10 in the BDI questionnaire, no anxiety (HADS A) with a median of 4.0, with 101 (83.5%) patients scoring lower than 8, nor pain-related catastrophizing (PCS median 4.0). According to the ISI questionnaire, they did not have clinically meaningful insomnia with a median score of 6.0 with 110 patients (90.9%) scoring lower than 15. We found no significant difference between different reconstruction types with regards to mood and sleep testing for BDI-II, HADS-A, HADS-D, PCS, and ISI. BDI-II was also controlled preoperatively.

The quality of life was comparable to the Finnish normative population. When comparing patients with different breast reconstructions, the quality of life did not show differences in general (p=0.14). An item of "role-physical" in RAND-36 showed lower scores in other types of reconstructions than DIEP or LD (Figure 3), but the difference did not reach statistical significance.

Discussion

Half of the breast reconstruction patients presented with CPSNP years after operation, with moderate to severe intensity in 14% of the patients. Preoperative pain prior to breast reconstruction correlated significantly with moderate to severe CPSNP. We found no significant difference in the prevalence of pain across different reconstruction types.

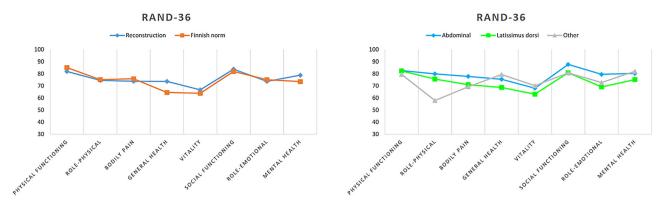


Figure 3: Line chart illustrating the scoring of patients in different RAND-36 items compared to Finnish normative population and different reconstruction types.

Generally, patients had recovered well, they had good quality of life and had no major problems in sleep or mood. Sensory loss was the major sensory finding in the operative area even years after operation. However, static allodynia, i.e. evoked pain for finger compression, was common in 55% of the patients.

Several methods for breast reconstruction exist, ranging from implants to various autologous flaps. In previous studies, autologous breast reconstructions have yielded higher patient reported satisfaction than implant-based reconstructions [8–12]. Some studies have also found higher patient reported satisfaction with DIEP and TRAM flaps compared to LD flaps [10, 11] and DIEP flaps compared to TRAM flaps [28, 29]. However, studies comparing different autologous reconstruction methods remain scarce. In our cohort, we confirmed the patient satisfaction for autologous compared with implant-based reconstructions according to quality of life physical measures in RAND-36.

Previous studies report that one fourth to half of women with breast reconstructions report persistent postoperative pain [15–17, 30] with 10–17% reporting moderate to severe pain [16, 31, 32]. This is in line with our results of moderate to severe CPSNP in 14% of patients. This percentage was at the same range of the overall moderate to severe postoperative pain prevalence (16%) of the larger breast cancer survivors' cohort at one year follow up after index operation and without reconstructions [33]. This suggests that reconstruction procedures do not worsen the postoperative pain prevalence. However, we found that preoperative pain in the operative area strongly correlated with moderate or severe CPSP. This is in line with previous evidence suggesting that preoperative pain significantly increases the risk of persistent postoperative pain [16, 34, 35].

Not much is known about the role of adjuvant therapies in pain susceptibility in reconstruction patients. It is well established that both radiotherapy and chemotherapy

may cause neuropathic pain [35–39]. However, the role of these in the development of neuropathic pain is not consistent in breast cancer survivors [19]. In our study, both radiotherapy and chemotherapy increased the incidence for evoked pain (p=0.039 and p=0.026, respectively), but not self-reported pain.

Previous studies have shown that sensory loss is a common adverse effect of breast reconstructions [40, 41]. Some spontaneous recovery of sensation has been described in the months following breast reconstruction. The reconstructed breast has shown persistent sensory loss in all reconstruction types [40]. In line with this, the surgical area was found to be hypoesthetic in our cohort.

Patient-reported quality of life has been shown to increase in patients with breast reconstruction compared with mastectomy alone [3–5, 42, 43]. This suggests that breast reconstruction, although a bigger operation with a longer recovery than in mastectomy, can effectively improve the quality of life, possibly by retaining the normal type of breast outlook.

In our cohort, quality of life (QoL) was similar to the Finnish normative population and had no differences in general between different reconstruction groups. The item "role-physical" in RAND-36 showed a trend for lower scores in other types of reconstructions than DIEP or LD. This is in line with previous body of literature suggesting that autologous tissue reconstructions lead to higher patient satisfaction [8–12].

No differences were found between reconstruction types with regards to mood, pain catastrophizing, or sleep. Previous studies have identified preoperative depression associating with worse outcomes in postmastectomy breast reconstruction [16, 44]. This underlines the clinical importance of identifying depression preoperatively. We found no difference in BDI-II or HADS scores between studied groups. Furthermore, BDI-II scores in our studied

population were similar to previously established normative populations [45]. It should be noted, however, that our study population significantly differs from the population in those normative studies with regards to age and gender. Likewise, in OoL, the item mental-health in RAND-36 showed similar scores in our patients compared to Finnish normative population.

A limitation of the study is the small number of patients in the reconstruction subgroups. Further, breast reconstruction may confirm a definitive diagnosis of neuropathic pain, but it does not establish causality. A strength of the study was a thorough clinical examination with detailed sensory testing and neuropathic pain grading. Further, this was a cross sectional substudy of a larger follow up cohort. Thus, we could utilize preoperative pain and other prospective data in addition to the research visit.

Conclusion

Moderate to severe pain occurred in 14% of the breast reconstruction patients, similar to that in patients after mastectomy, without reconstruction. The frequency of CPSNP did not differ between different types of reconstruction surgery. This information is useful when informing the patient about the possible complications following breast reconstruction surgery.

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Ethics Approval: The Coordinating Ethics Board of the Helsinki and Uusimaa Hospital District approved the study and it was registered in ClinicalTrials.gov (NCT02487524).

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