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Hyperesthesia one year after breast augmentation surgery increases the odds for persisting pain at four years
A prospective four-year follow-up study

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ABSTRACT

In this long-term follow-up study of 175 women, we investigated the prevalence of and factors associated with persisting pain and sensory changes four years after augmentation mammoplasty. Previously the women had participated in an acute postoperative pain study, and follow-up investigations at 6 weeks and 1 year after surgery. In the present study, the women were mailed questionnaires about pain, sensory changes, and affection of daily life, quality of life and pain catastrophizing 4 years after surgery.

One hundred and sixteen women answered the questionnaire. The fraction of women reporting evoked- and/or spontaneous pain during the last 24 h had declined from 20% at 1 year to 14% at 4 years. Hyperesthesia had declined from 46% at 1 year to 32% at 4 years, while the change in hypoesthesia was small, 47% at 1 year to 51% at 4 years. Methylprednisolone and parecoxib given preincisionally reduced acute postoperative pain and reduced the prevalence of hyperesthesia after 6 weeks/1 year, but after 4 years we found no significant differences between the test drug groups. Those having concomitant pain and hyperesthesia at 6 weeks and 1 year had high odds for persisting pain at 4 years (OR 7.8, 95% CI 2.1–29.8, $P = 0.003$; OR 13.2, 95% CI 2.5–71.3, $P = 0.003$). In patients without pain but with hyperesthesia at 1 year, the hyperesthesia increased the odds for pain at 4 years (OR 2.6 95% CI 1.1–6.1, $P = 0.03$). Hypoesthesia at 6 weeks or at 1 year did not affect the odds for pain at 4 years. A good general health condition (mental and physical) was associated with reduced odds for pain at 4 years (OR = 0.56, 95% CI 0.35–0.88, $P = 0.01$). However, using the Short Form health survey, SF-12, the Mental Component Summary Score seemed to affect the odds for chronic pain more than the Physical Component Summary Score.

To conclude, the prevalence of pain and hyperesthesia after breast augmentation declined from 1 to 4 years. Nevertheless, the most striking finding in the current trial was that pain coinciding with hyperesthesia at 6 weeks and 1 year resulted in highly increased odds for persistent postoperative pain. Even hyperesthesia alone, without pain, increased the odds for chronic postsurgical pain. Thus, the present study suggests hyperesthesia as an independent risk factor for chronic postsurgical pain.

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1. Introduction

Chronic postoperative pain, defined as pain persisting beyond 3 months after surgery, is now accepted as an important negative outcome of surgery and occurs in up to 75% of surgical patients, depending on the type of surgery [1–4]. After breast cancer surgery, 13–68% of patients suffer from chronic pain [5,6].

In the US alone, 400.000 cosmetic augmentation mammoplasties are performed each year and the number of such operations increases every year [7]. After augmentation mammoplasty, the prevalence of persistent pain in retrospective studies has varied from 18 to 50% [8–10]. The only prospective study that has been published in a medical journal, revealed a prevalence of non-evoked and evoked pain after 1 year of 13 and 20% [11,12]. That study also found 47% to have hypoesthesia and 46% to have hyperesthesia. Previous reports on sensory deficits after augmentation mammoplasty are conflicting and the conclusions varies from a negligible effect on sensory function to sensory impairment in all patients [13,14].

Previously, large long-term follow-up retrospective studies (901 and 1264 patients included) have demonstrated pain rates of 5–16% at 3 years and 7–17% at 5 years [15]. These numbers may indicate that the pain after augmentation mammoplasty does not follow the natural declining course of chronic pain seen after other types of surgery [16]. However, long-term prospective follow-up studies on pain and sensory changes after augmentation mammoplasty have not been done previously. During the recent years, there has been a shift of emphasis away from plain number counting to the examination of risk factors and prevention of chronic postoperative pain. In our study from 2006 we found acute pain, and pain and hyperesthesia at 6 weeks to be positively associated with pain and hyperesthesia at 1 year. We also found that methylprednisolone given preincisionally reduced hyperesthesia at 1 year [12]. The aims of the present study were thus to follow-up the175 women who responded at 6 weeks and 1 year and to study the prevalence of pain and sensory changes four years after augmentation mammoplasty, and their impact on quality of life and activities of daily living. We also wanted to investigate if pain, sensory changes, quality of life and activities of daily living were positively or negatively associated with persisting pain at 4 years, and if a preincisional dose of parecoxib, methylprednisolone or placebo could have any effect on persisting pain or hyperesthesia at 4 years.

2. Methods

2.1. Design

This study was a long-term follow-up of 175 women, who underwent cosmetic breast augmentation surgery four years ago, and had participated in a single-centre, prospective, randomized, double blind, single-dose, and parallel-group acute pain trial and a follow-up study at 6 weeks and 1year. In the acute postoperative pain study we compared intravenous administration of methylprednisolone 125 mg ($n = 56$) with parecoxib 40 mg ($n = 57$) and placebo (saline) ($n = 62$) immediately before breast augmentation surgery.

In the follow-up study at 6 weeks and 1year, the women were mailed questionnaires about pain, sensory changes, and affection of daily life. The acute pain and the 1-year follow-up study were published in 2006 [11,12]. In the present 4-year follow-up study, the questionnaires were largely identical to the questionnaires used at the 6 week and 1 year, but more comprehensive concerning quality of life and pain catastrophizing.

2.1.1. Patient inclusion

After approval from the National Committee for Research Ethics in Norway, Region South-east, and The Norwegian Data Inspectorate, the 175 women that responded to the 1 year questionnaire, were mailed a new questionnaire with stamped and addressed return envelopes. All patients received detailed written instructions for correct completion of the questionnaires. Three attempts by mail were made to reach those who did not send back the completed questionnaires.

2.2. Assessment of outcomes

The primary outcome variable was the prevalence of pain at 4 years. Secondary outcome variables were the prevalence of sensory changes.

2.2.1. Pain

In the acute pain study we assessed the effect of the test drugs on non-evoked and evoked pain at 1, 2, 4 and 6 h after surgery, and in the morning and evening the first six days after surgery using an 11-point numeric rating scale (0–10 NRS, 0 = no pain and 10 = unbearable pain) [11].

In the follow-up study at 6 weeks and 1 year, and in the present follow-up study at 4 years, we asked the women to register pain at rest and evoked pain at present, during the last 24 h, during the last week, and to rate the pain on a 0–10 NRS. We also asked about the worst pain experienced the last week. The women registered degree of functional impairment of activities of daily living due to pain on a 0–10 NRS. In the present study, those who reported pain were asked to categorize their pain according to the Scandinavian version of the McGill short form. This version has been validated in Scandinavia and consists of ten descriptive and five affective terms describing different possible aspects of their pain experience rating each term on a 4 categories 0–3 scale where 0 = no pain, 1 = mild pain, 2 = moderate pain and 3 = severe pain [17]. The women were instructed only to report pain and sensory changes they thought were related to their cosmetic breast surgery.

2.2.2. Sensory changes

We wanted to measure sensory hypo- and hyperphenomena in and around the scar. We decided not to use the terms “hyperalgesia” or “allodynia”, but “hyperesthesia” explained as hypersensitivity in the skin in or around the scar. The women found this term easier to interpret. According to IASP pain terminology hyperesthesia is defined as increased sensitivity or increased response to stimuli, and hypoesthesia is defined as decreased sensitivity or decreased response to stimuli [18]. In the present trial, all stimuli were cutaneous. Subjective tactile hyperesthesia or hypoesthesia was determined by asking the patient to stroke a finger over an area from below the scar and up, including the nipple, comparing the sensation with the abdominal skin.

Different aspects of subjective hyperesthesia like hypersensitivity to touch, pressure, cold and warmth, from clothes, and from showering, were noted on a 0–3 verbal rating scale (VRS, 0 = no, 1 = mild, 2 = moderate, 3 = strong). We also included a question about dysesthesia; whether or not they experienced itching, a burning sensation or unfamiliar/strange responses to cutaneous stimuli.

2.2.3. Physical and mental health/quality of life

We used the Short Form 12-item Health Survey (SF-12); a general health related quality of life questionnaire comprising 12 questions about physical functioning, bodily pain, general health, vitality, social functioning, mental health, and the impact physical

and mental health has on daily life. The survey is validated for the Norwegian population [19,20]. We calculated 2 summary scores, Physical Component Summary (PCS) and Mental Component Summary (MCS), from the results of SF-12. The summary scores were derived by converting each item response into both physical and mental standardized values. These values have been standardized to give mean score of 50 according to the mean for a large US female population [21].

2.2.4. Pain catastrophizing

We used the 13-item Pain Catastrophizing Scale where patients are asked to rate statements concerning their cognitive and affective reactions to pain on a 0–5 point scale. A Pain Catastrophizing Scale Sum Score was calculated from all items (range 0–65), where high sums score indicated a high level of catastrophizing ([1,22]). The different items of the Pain Catastrophizing Scale were further categorized into 3 components: rumination, magnification and helplessness [22]. The Pain Catastrophizing Sum Score and the three main components of this score were compared with the scores of a normal US female population [22].

2.3. Statistical analyses

Demographic data were analyzed by one-way analysis of variance (one-way ANOVA).

Descriptive statistics are given in frequencies and percentages. The dichotomous data were analyzed with the Fisher's exact test. Kruskal–Wallis and subsequent Mann–Whitney *U* test were used to analyze the pain and hyperesthesia data with four or more categories. Logistic regression analysis was used to determine which variables that was associated with chronic spontaneous pain, evoked pain, hyperesthesia and hypoesthesia. Multiple linear regression analysis could not be used because the dependent variables were either dichotomous or had skewed distributions. Significance was determined at the $P < 0.05$ level.

The IBM SPSS/PASW statistical program, version 18.0 (SPSS Inc., IL, USA) was used for analyses of all data.

2.4. Sample size

Sample size was primarily calculated for the acute pain study [11]. Fifty-four patients per each of the three groups were calculated to give sufficient power to find clinically important differences between the treatment groups. We calculated that a response $N = 159$ would give a two-sided 95% confidence interval for a single proportion that would extend 0.034–0.078 from the observed proportion for expected proportions between 0.05 and 0.95. In the 1-year follow-up study 175 women answered the questionnaires. In the 4-year follow-up study, the differences between the drug groups were of minor interest due to power consideration. Even with 100% response rate ($N = 175$) a difference of 50% in presence of clinical characteristics like pain and hypersensitivity would only be detected with a power of 32% (SPSS Sample Power version 2.0). In order to be able to find convincing positive or negative associations between pain at 4 years and variables in the acute postoperative phase, at 6 weeks and 1 year using logistic regression, the minimum number of cases to include, based on the work of Peduzzi et al. [23] was: 10/proportion of cases with pain = 10/0.14 = 71. However, if the resulting number is less than 100, the sample size should be increased to 100 as suggested by Long [24]. In addition, in order to obtain satisfactory representativeness of the target population we needed response from at least 60% (105 of the 175 included women) [25].

Table 1
Baseline data of all patients that entered the study.

Age, year	33 ± 7
Weight, kg	59 ± 7
Height, cm	168 ± 6

Data are mean ± SD.

3. Results

3.1. Demographic data

The participants had similar distribution of age, weight and height (Table 1). Four years previously, all patients had undergone similar type of surgery and anaesthesia.

3.1.1. Patient flow

All the 175 respondents in the 6 weeks and 1-year follow-up study were included in the 4-year follow-up study. At 4 years, 116 women (66%) completed and sent back the questionnaire.

3.2. Effect of preincisional test drugs 4 years after surgery

All patients were given methylprednisolone 125 mg ($n = 56$), parecoxib 40 mg ($n = 57$) or placebo (saline) ($n = 62$) i.v. immediately before surgery. At 1 year those receiving methylprednisolone had significantly less hyperesthesia compared with placebo. At 4 years no significant differences in any variables were found between the drug groups (Kruskal–Wallis test). However, the number of respondents at 4 years was too small to give appropriate study power in order to find differences between the drug groups. With 116 respondents we had a power of 23% to detect a reduction in the incidence of 50% (SPSS Sample Power version 2.0).

3.3. Pain 4 years after surgery

Compared with the fraction of women reporting evoked- and/or spontaneous pain during the last 24 h at 1 year (24%), the fraction at 4 years was declined to 14%. The pain was mostly mild, 13% had pain ranging from 1 to 3 (NRS 0–10), 1% reported pain from 4 to 6 and nobody reported pain ≥7. When reporting worst pain during the last week, the fraction with pain ≥1 was somewhat larger, 20%, but had declined from 33.6% at 1 year. The fraction scoring ≥1 on any of the NRS pain scores was 22.4% at 4 years and had decreased from 33.1% at 1 year. The fraction of women scoring on the NRS and/or the McGill score was 36% (Tables 2 and 4).

Four women (3%) had sought medical support because of pain from the operated area. Pain related to strenuous physical exercise was experienced by 13%. Most of the patients reported a minor

Table 2
Prevalence of pain 4 years after breast augmentation surgery. Number and percentage of patients categorized according to pain intensity on the 0–10 NRS.

	Pain intensity on the 0–10 NRS			
	0	1–3	4–6	7–10
Pain at rest the last 24 h	104 90%	12 10%	0 0%	0 0%
Evoked pain the last 24 h	100 86%	15 13%	1 1%	0 0%
Pain at rest the last week	98 85%	17 15%	0 0%	0 0%
Evoked pain the last week	97 85%	15 13%	2 2%	0 0%
Worst pain the last week	92 80%	21 18%	2 2%	0 0%

Table 3
The Short-form McGill Pain Questionnaire. Number and percentage of patients categorized according to pain intensity described by the use of Short-form McGill Pain Questionnaire on a 4 categories 0–3 scale where 0 = no pain, 1 = mild pain, 2 = moderate pain and 3 = severe pain.

Pain descriptors	Pain intensity			
	None	Mild	Moderate	Severe
A. Sensory pain descriptors				
Throbbing	111 96.5%	4 3.5%	0 0%	0 0%
Shooting	108 93.9%	4 3.5%	2 1.7%	1 0.9%
Stabbing	87 75.7%	23 20%	4 3.5%	1 0.9%
Sharp	112 97.4%	2 1.7%	0 0%	1 0.9%
Cramping	112 97.4%	3 2.6%	0 0%	0 0%
Gnawing	111 96.5%	3 2.6%	0 0%	1 0.9%
Hot-burning	109 94.8%	5 4.3%	1 0.9%	0 0%
Aching	106 92.2%	9 7.8%	0 0%	0 0%
Heavy	108 93.9%	3 2.6%	3 2.6%	1 0.9%
Tender	100 87.0%	12 10.4%	0 0%	3 2.6
Splitting	109 94.8%	4 3.5%	1 0.9%	1 0.9%
B. Affective pain descriptors				
Tiring-exhausting	113 98.3%	1 0.9%	1 0.9%	0 0%
Sickening	114 99.1%	1 0.9%	0 0%	0 0%
Fearful	115 100%	0 0%	0 0%	0 0%
Punishing-cruel	113% 98.3%	2 1.7%	0 0%	0 0%

The total number of women answering the Short-form McGill questionnaire was 115.

influence on daily activities: 11% reported NRS 0–3, one woman (0.9%) had NRS = 5 and another (0.9%) had NRS = 7. These numbers were very similar to the numbers at 1 year where activities of daily living were affected by pain in 14% of the patients.

Among the 116 that responded at 4 years, 95 reported no pain on the NRS scores at 1 year. Of these 95 respondents reporting no pain at 1 year, 10.5% reported pain at 4 years. Twenty-one of the 116 respondents at 4 years reported pain at 1 year. Of these 21, 48% had no pain at 4 years.

3.4. The short form—McGill questionnaire

35% of the women reported pain using at least one pain descriptor from the SF-McGill questionnaire. All of these (34.8%) scored on the sensory McGill categories, while only 2.6% scored on the affective categories. The two categories most frequently used were stabbing pain (24%) and tenderness (13%) (Table 3).

3.5. Sensory changes 4 years after surgery

Like at 1 year, the sensory deficits described at 4 years were still consistent with injury to the lateral and cutaneous branches of the third, and/or fourth, and/or fifth intercostal nerves. Hyperesthesia was present in 32% at 4 years and had decreased from 46% at 1 year.

Dysesthesia was reported by 34%. Concerning the different modalities of hyperesthesia, 24% was hypersensitive to touch, 22% had pressure–hyperesthesia, 15% had cold hyperesthesia, 6% had heat hyperesthesia and 20% were hypersensitive to shower/water or clothes (Table 4).

Among the 116 that responded at 4 years, 61 (52%) reported no hyperesthesia at 1 year. Of these reporting no hyperesthesia at 1 year, 13% reported hyperesthesia at 4 years. Fifty-five of the 116 respondents at 4 years reported hyperesthesia at 1 year. Of these, 42% had no hyperesthesia at 4 years. The prevalence of hypoesthesia did not change much, but was somewhat increased from 46% at 1 year to 51% at 4 years.

3.6. The short form 12-item health survey (SF-12)

The mean Physical Component Summary Score (PCS) of the SF-12 was 55.5 (SD ± 5) and the mean Mental Component Summary Score (MCS) was 49.4 (SD ± 10). These values are close to those found in a Norwegian normal female population. The mean value for a Norwegian normal female population is 50.3 (SD ± 8.8) for PCS and 50.6 (SD ± 9.9) for MCS (21). While 4.4% of the respondents reported "poor" or "fairly good" general health, 95.6% reported "good" or "excellent" general health. Six percent of the women accomplished less than they wanted because of limitations due to reduced physical health. Twenty percent accomplished less than wanted because of impaired mental health. Social functioning was affected by physical and/or mental health problems in 20%. Sixty-three percent felt downhearted and blue at least some of the time. Nine percent felt a constant lack of mental energy and 14% felt that they never, or only now and then, were calm and peaceful (Tables 5 and 6).

3.7. Pain catastrophizing

The mean Pain Catastrophizing Total Score was 9.7 (SD ± 8). In a normal US female population, this score is 15.68 (SD ± 10.93). The mean subscale scores were: Rumination 4.65 (SD ± 3.9); Magnification 2.02 (SD ± 1.9); Helplessness 2.96 (SD ± 3.24). In a normal US female population, these scores are: Rumination 6.75 (SD ± 4.32); Magnification 3.32 (SD ± 2.46); Helplessness 5.62 (SD ± 5.14). The fraction of respondents scoring on the Pain Catastrophizing Scale summary score was 81%. The scores ranged from 0 to 35 on a possible summary score scale from 0 to 65.

3.8. Factors associated with persisting pain at 4 years

No associations between acute pain during the first postoperative hours, during the first six postoperative days, acute rescue analgesic usage, and pain at 4 years were revealed.

Variables measured 6 weeks after surgery associated with increased odds for having pain in the operated area at 4 years were: non-evoked and evoked pain, and hyperesthesia (Table 6).

Variables measured 1 year after surgery associated with increased odds for persisting postsurgical pain at 4 years, were: non-evoked and evoked pain, hyperesthesia, and the presence of hyperesthesia alone without the presence of pain (Table 6).

Those having concomitant pain and hyperesthesia at 6 weeks and one year had high odds for persisting pain at 4 years (OR 7.8, 95% CI 2.1–29.8, $P = 0.003$; OR 13.2, 95% CI 2.5–71.3, $P = 0.003$). Pain without hyperesthesia at 6 weeks or 1 year did not increase the odds for pain at 4 years. Hyperesthesia without the presence of pain at 1 year increased the odds for pain at 4 years (OR 2.6 95% CI 1.1–6.1, $P = 0.03$). Hypoesthesia at 6 weeks or at 1 year did not

Table 4
Pain and sensory disturbances.

	Day 1	Day 6	6 weeks	1 year	4 years
A. Fractions of patients reporting non-evoked/evoked pain using 0–10 NRS and pain using pain descriptors from the Short-form McGill Pain Questionnaire at day 1, day 6, 6 weeks, 1 year and 4 years after surgery, and at least any type of pain in the operated area after 4 years					
Pain (McGill)	*	*	60%	50%	35%
Pain (NRS)	100%	78%	36%	24%	14%
Pain (any type)	*	*	*	*	36%

	6 weeks	1 year	4 years
B. Fractions of patients with sensory changes at day 1, day 6, 6 weeks, 1 year and 4 years after surgery			
Hyperesthesia	46%	45%	32%
Hypoesthesia	47%	46%	51%
Dysesthesia	*	*	34%

Modality↓ or intensity→	None	Mild	Moderate	Severe
C. Fractions of patients reporting hyperesthesia categorized according to modality and intensity 4 years after surgery				
Touch	75.4%	18.4%	5.3%	0.9%
Pressure	78.1%	9.6%	12.3%	0.0%
Cold	85.1%	7.0%	3.5%	4.4%
Heat	93.9%	6.1%	0.0%	0.0%
Clothes/shower	79.8%	14.9%	4.4%	0.9%

Table 5
The short form 12-item health survey (SF-12).

	A. Numbers and percentages of respondents categorized according to answers given in the SF-12 questionnaires				
	Poor	Fair	Good	Very good	Excellent
1. General health	2 1.8%	3 2.6%	24 21.1%	47 41.2%	38 33.3%

	Limited a lot	Limited a little	Not limited at all
2. Moderate activities	0 0%	6 5.3%	107 94.7%
3. Climbing several flights of stairs	2 1.8%	8 7.1%	103 91.2%

	Yes	No
4. Accomplished less than you like as a result of physical health	7 6.2%	106 93.8%
5. Limited in the kind of work or other activities as a result of physical health	2 1.8%	111 98.2%
6. Accomplished less than you like as a result of any emotional problems	23 20.4%	90 79.6%
7. Did not do work as carefully as usual as a result of any emotional problems	2 1.8%	111 98.2%

	Not at all	A little bit	Moderately	Quite a bit	Extremely
8. How much did pain interfere with normal work	101 89.4%	9 8.0%	2 1.8%	1 0.9%	0 0%

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
9. Calm and peaceful	16 14.3%	38 33.9%	25 22.3%	17 15.2%	14 12.5%	2 1.8%
10. A lot of energy	7 6.3%	28 25.2%	27 24.3%	23 20.7%	16 14.4%	10 9%
11. Downhearted and blue	1 0.9%	2 1.8%	10 9%	14 12.4%	44 38.9%	42 37.2%
12. Physical health or emotional problems interfering with social activities	1 0.9%	1 0.9%	6 5.3%	7 6.2%	8 7.1%	90 79.6%

B. Physical and mental health summary scores calculated from the SF-12 questionnaire

Summary scores	Breast augmentation population	Normal Norwegian female population
Physical Component Summary Score (PCS)	55.5 (SD ± 5)	50.3 (SD ± 8.8)
Mental Component Summary Score (MCS)	49.4 (SD ± 10)	50.6 (SD ± 9.9)

Table 6

Factor	Odds ratio	95% CI	*P*-value
A. The affection of pain and sensory variables on the odds for pain 4 years after surgery			
Non-evoked pain at 6 weeks	2.7	1.2–6.4	0.02
Evoked pain at 6 weeks	5.1	2.2–11.8	0.0002
Hyperesthesia at 6 weeks	2.4	0.9–6.3	NS
Concomitant pain and hyperesthesia at 6 weeks	7.8	2.1–29.8	0.003
Hyperesthesia without pain at 6 weeks	1.3	0.5–3.0	NS
Non-evoked pain at 1 year	6.5	1.5–28.1	0.01
Evoked pain at 1 year	10.8	2.6–44.0	0.001
Hyperesthesia at 1 year	6.3	2.2–17.8	0.001
Concomitant pain and hyperesthesia at 1 year	13.2	2.5–71.3	0.003
Hyperesthesia without pain at 1 year	2.6	1.1–6.1	0.03
Hyperesthesia at 4 years	5.2	2.2–12.2	0.0002
B. Physical and mental health factors affecting the odds for persisting pain 4 years after surgery			
SF-12 general health	0.56	0.35–8.8	0.01
SF-12 health interference of social function	3.5	1.8–6.7	0.0002
SF-12 Mental Component Summary Score	0.91	0.8–0.9	0.0001
SF-12 feeling downhearted and blue	2.2	1.5–3.5	0.0003
SF-12 feeling calm and peaceful	0.53	0.38–0.75	0.0003
SF-12 accomplished less due to emotional problems	3.9	1.5–10.2	0.005
SF-12 feeling a lot of energy	0.59	4.4–8.2	0.001
Pain catastrophizing-magnification	1.3	1.1–1.5	0.04

affect the odds for pain at 4 years. A good general health condition (mental and physical) was associated with reduced odds for pain at 4 years (OR 0.56, 95% CI 0.35–0.88, $P = 0.01$).

At 4 years the presence of hyperesthesia was associated with concomitant pain (OR 5.2, 95% CI 2.2–12.2, P = 0.0002). (Table 6). The Mental Component Summary score (MCS) derived from SF-12 was negatively associated with persistent pain at 4 years (OR 0.91 CI 0.8–0.9, $P = 0.0001$) (i.e. the better mental health score, the lesser pain). The Physical Component Summary score (PCS) did not have a significant association with persistent postoperative pain in the current study (OR 0.95 CI 0.88–1.03).

While the Pain Catastrophizing Total Score did not significantly affect the odds for chronic pain at 4 years, one of the Pain Catastrophizing subscale scores, namely magnification was associated with a significant increase in the odds for chronic postoperative pain (OR 1.3 CI 1.1–1.5, $P = 0.04$). The two other Pain Catastrophizing subscale scores, rumination and helplessness did not affect the odds for chronic pain. Hypoesthesia at 6 weeks and 1 year and the presence of hypoesthesia at 4 years, did not affect the odds for pain at 4 years.

4. Discussion

The present study demonstrates that chronic postoperative pain after breast augmentation surgery fades with time. The fractions of women reporting pain during the last 24 h (NRS) were reduced from 20% at 1 year to 14% at 4 years. This is in concert with previous long-term follow-up studies after breast cancer surgery [26]. In that study the proportion reporting pain 3 years after surgery was reduced from 43% at 3 years till 17% at 9 years.

In large-scale studies after breast augmentation 5–16% had pain at 3 years and 7–17% at 5 years [15]. Some of these studies indicate that pain after augmentation mammoplasty do not fade, but is relatively stable or even increases with time. One proposed reason for this is capsular contractures setting nerves on stretch due to foreign body reaction [8,9]. Correspondingly, we found that 10 of the 95 women that did not report pain at 1 year reported pain 3 years later. Whether this is due to a surgery specific reaction like capsular contraction or simply due to inconsistent reporting, cannot be answered by this study.

In the present study, the pain was mostly mild and only 1% had pain intensity >4 on a 0–10 NRS scale. However, more than a million augmentation procedures were done in 2008 worldwide, and cosmetic breast augmentation has shown an increase from 32.607 in 1992 to 355.671 in 2008 in the US only [7]. Thus, the number of women suffering from chronic pain after cosmetic breast augmentation might be considerable.

It is interesting that while 22.4% reported pain during the last week, 35% described their pain by sensory and/or affective descriptors from the Short Form McGill Pain Questionnaire. We saw the same phenomenon at 1 year where 33.1% reported pain during the last two weeks and 49.7% scored on the McGill Pain Questionnaire. The main reason for this may be that sensory disturbances are very common after this type of surgery, and that the transition from a sensory disturbance without pain to a sensory disturbance with pain is not sharp. Another reason is that it may be easier to evaluate pain with descriptive words compared with a 0–10 NRS. However, compared with McGill Pain Questionnaire, NRS has demonstrated better validity and should be the preferred pain scale [27].

Hypoesthesia did not change much from 1 year (47%) to four years (51%) indicating total transection and/or irreversible damage of nerves as the cause of reduced sensitivity. On the contrary, the prevalence of hyperesthesia was reduced from 46% at 1 year to 32% at 4 years. This could be due to repaired nerve function in partial damaged nerves, or reduced central sensitization with time after surgery.

The summary scores on the physical and mental components of SF-12 and the Pain Catastrophizing Scale indicate that the women had a good physical and mental health and their tendency to catastrophize was lower compared to a normal female population. However, scores on these questionnaires indicated associations between mental health/psychosocial variables and persisting pain at 4 years. A high Mental Component Summary score was associated with reduced odds for pain at 4 years. As we only have mental- and physical health data measured four years after surgery, it is difficult to know whether mental health factors affect the likelihood for chronic postoperative pain, or if the presence of pain affect mental health. Both statements might be true. In future studies, a preoperative mental and physical health status would be of interest.

The most striking finding in this study was that pain with concomitant hyperesthesia at 6 weeks and 1 year, markedly increased the odds for persistent postoperative pain at four years. Hyperesthesia *without* the presence pain at 1 year was associated with increased odds for persistent postoperative pain at 4 years. This is the first clinical long-term follow-up study of chronic postoperative pain that clearly points out reported hyperesthesia as an independent risk factor for developing chronic pain. The fractions of

patients reported pain but not hyperesthesia at 6 weeks and 1 year was too low (3.4% and 4.6%) to calculate any valid odds ratios. Thus, the present study was not able to demonstrate pain alone, without the presence of hyperesthesia, as an independent risk factor for chronic postsurgical pain. The present study convincingly demonstrated that pain present together with hyperesthesia is strongly associated with persistent postoperative pain (OR 13.2). Persistent pain and hyperesthesia reported by our patients indicate partial peripheral nerve damage and central sensitisation in the spinal cord dorsal horn, while hypoesthesia can indicate a more complete peripheral nerve injury [28,29].

Acute and prolonged acute pain has been proposed as an independent risk factor for chronic pain [30,31]. However, is there evidence for a causal relationship? The present study indicates that this is not necessarily true. The current trial did not reveal any association between acute postoperative pain during the first hours after surgery, or during the first six postoperative days, and pain at 4 years. Acute and chronic pain could be separate consequences of injury [32]. In a study by Lavand'homme et al. [33] the area of secondary hyperalgesia around a surgical wound, but not postoperative pain scores, influenced the presence of pain one year after surgery. Although there is consensus that the intensity of early postoperative pain may predict the risk of developing persistent postoperative pain [30], studies of various analgesic techniques have failed to document a relation between the reduction of acute postoperative pain and persistent pain [34]. Numerous attempts have been made to establish an analgesic regime that prevents CPSP, so far without convincing results. In the acute part of our study, the administration of glucocorticoids, parecoxib or placebo, the active drugs gave lower pain scores in the acute postoperative period, and methylprednisolone reduced hyperesthesia which was associated with less pain one year after surgery [11,12]. No differences between the drug groups were seen after four years, but this might be due to lower power in the 4-years follow-up.

This study clearly shows that hyperesthesia increases the odds for persistent postsurgical pain. According to our findings, acute and chronic postoperative pain can be considered two different entities. In the future, studies investigating the prevention of chronic postoperative pain should also aim at reducing central plastic changes, as the reduction of mere acute postoperative pain does not seem to bee associated with less persistent pain. Early identified risk subjects could be candidates for more intense secondary prevention with a multidisciplinary approach including "antihyperalgesic" pharmacological treatment.

It is evident that the easiest path to prevent CPSP is to avoid surgery, especially when this is not indicated by medical causes [4]. All patients considering cosmetic breast augmentation should be informed about the risk of persistent pain and sensory disturbances.

In conclusion, even though the prevalence of pain and hyperesthesia after breast augmentation declined from 1 to 4 years, a considerable group of subjects (13%) still had postsurgical pain 4 years after breast augmentation surgery. The most striking finding in the current trial was that pain coinciding with hyperesthesia at 6 weeks and 1 year resulted in highly increased odds for persistent postoperative pain, and hyperesthesia was recognized as an independent risk factor. The subjects at highest risk for CPSP can be identified as early as six weeks after surgery after surgery as patients with both pain and hyperesthesia.

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