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THE EFFECTS OF REDUCTION MAMMAPLASTY

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Academic Dissertation

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“Three grand essentials to happiness in this life are something to do,
something to love, and something to hope for.”

Joseph Addison (1672–1719)

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1 LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the original articles listed on this page. They are referred to in the text by their Roman numerals.

- I Saariniemi KM, Keränen UH, Salminen-Peltola PK, Kuokkanen HO. Reduction mammoplasty is effective treatment according to two quality of life instruments. A prospective randomised clinical trial. *J Plast Reconstr Aesthet Surg* 61:1472-1478, 2008.
- II Saariniemi KM, Sintonen H, Kuokkanen HO. The improvement in quality of life after breast reduction is comparable to that after major joint replacement. *Scand J Plast Reconstr Surg Hand Surg* 42:194-198, 2008.
- III Saariniemi KM, Joukamaa M, Raitasalo R, Kuokkanen HO. Breast reduction alleviates depression and anxiety and restores self-esteem: A prospective randomised clinical trial. *Scand J Plast Reconstr Surg Hand Surg* 43:320-24, 2009.
- IV Saariniemi KM, Luukkaala T, Kuokkanen HO. The outcome of reduction mammoplasty is affected more by psychosocial factors than by the changes in breast dimensions. *Scand J Surg* 2010 (accepted).
- V Saariniemi KM, Kuokkanen HO, Tukiainen EJ. The outcome of reduction mammoplasty remains stable at 2–5 years' follow-up: A prospective study. *J Plast Reconstr Aesthet Surg* doi:10.1016/j.bjps.2010.09.010, 2010 (in press).

2 ABBREVIATIONS AND SYNONYMS

| | |
|-----------------------|---|
| Reduction mammoplasty | Breast reduction, reduction mammoplasty |
| Breast hypertrophy | Macromastia |
| Intertrigo | Rash in body folds (in this case under the breast) |
| Bottoming-out | Pseudoptosis, descend of inferior breast and upward rotation of the nipple |
| Ptosis | Descend of the nipple (and the breast) |
| HRQoL | Health Related Quality of Life |
| Health burden | Health deficit, loss of quality of life |
| QALY(s) | Quality-adjusted life year(s) |
| Cost-utility analysis | Analysis of cost per QALY: in medicine the term is often used interchangeably with cost-effectiveness |
| SF-36 | Short Form-36 quality of life questionnaire |
| SF-6D | Single index score of SF-36 |
| PCS | Physical summary score of SF-36 |
| MCS | Mental summary score of SF-36 |
| 15D | 15D quality of life questionnaire |
| 15D score | Single index score of 15D |
| FBAS | Finnish Breast-Associated Symptoms questionnaire |
| FPQ | Finnish Pain Questionnaire |
| RBDI | Raitasalo's modification of the Beck Depression Inventory (BDI) |
| BRSQ | Breast-Related Symptoms Questionnaire |
| RCT(s) | Randomised controlled trial(s) |

3 ABSTRACT

Background

Symptomatic hypertrophic breasts cause a health burden with physical and psychosocial morbidity. The value of reduction mammoplasty in the treatment of symptomatic breast hypertrophy has been consistently reported by patients and has been well recognised by plastic surgeons for a long time. However, the scientific evidence of the effects of reduction mammoplasty has been weak or lacking.

During the design of this study most of the previous studies were retrospective and the few prospective studies had methodological limitations. Therefore, an obvious need for prospective randomised studies was present. Nevertheless, practical and ethical considerations seemed to make this study design impossible, because the waiting time for the operation was several years. The legislation and subsequent introduction of the uniform criteria for access to non-emergency treatment in Finland removed these obstacles, as all patients received their treatment within a reasonable time. As a result, a randomised controlled trial with a six-month follow-up time was designed and conducted. In addition, a follow-up study with two to five years' follow-up was also carried out later. The effects of reduction mammoplasty on the patients' breast-related symptoms, psychological symptoms, pain and quality of life was assessed. In addition, factors affecting the outcome were investigated.

Patients and Methods

This study was carried out in the Hospital District of Helsinki and Uusimaa, Finland. Eighty-two out of the approximately 300 patients on the waiting list in 2004 agreed to participate in the study. Patients were randomised either to be operated (40 patients) on or to be followed up (42 patients). The follow-up time for both groups was six months. The patients were operated on by plastic surgeons or trainees at the Department of Plastic Surgery at Helsinki University Central Hospital or at the Department of Surgery at Hyvinkää Hospital. The patients completed five questionnaires: the SF-36 and the 15D quality of life questionnaires, the Finnish Breast-Associated Symptoms questionnaire (FBAS), a mood questionnaire (Raitasalo's modification of the short form of the Beck Depression Inventory, RBDI), and a pain questionnaire (The Finnish Pain Questionnaire, FPQ). Sixty-two out of the original 82 patients agreed to participate in the prospective follow-up study. In this study, patients completed the 15D quality of life questionnaire, the Finnish Breast-Associated Symptoms questionnaire, and the RBDI mood questionnaire.

Results

After six months' follow-up, patients who had undergone reduction mammoplasty had a significantly better quality of life, fewer breast-associated symptoms and less pain, and they were less depressed or anxious when compared to patients who had not undergone surgery. The change in quality of life was more than two times the

minimal clinically important difference. The patients' preoperative quality of life was significantly inferior when compared to the age-standardised general population. This health burden was removed with reduction mammoplasty. The health loss related to symptomatic breast hypertrophy was comparable to that of patients with major joint arthrosis. In terms of change in quality of life, the intervention effect of reduction mammoplasty was comparable to that of hip joint replacement and more pronounced than that of knee joint replacement surgery. The outcome of reduction mammoplasty was affected more by preoperative psychosocial factors than by changes in breast dimensions. The effects of reduction mammoplasty remained stable at two to five years' follow-up.

Conclusions

In terms of quality of life, symptomatic breast hypertrophy causes a considerable health loss comparable to that of major joint arthrosis. Patients who undergo surgery have fewer breast-associated symptoms and less pain, and they are less depressed or anxious and have an improved quality of life. The intervention effect is comparable to that of major joint replacement surgery, and it remains stable at two to five years' follow-up. The outcome of reduction mammoplasty is affected by preoperative psychosocial factors.

4 INTRODUCTION

The value of reduction mammoplasty in the treatment of symptomatic breast hypertrophy has been consistently reported by patients and has been well recognised by plastic surgeons for a long time. Symptomatic hypertrophic breasts cause a health burden with physical and psychosocial morbidity, affecting the patients' quality of life. This condition can be treated by reducing the weight of the heavy breasts. The physical symptoms reported by patients include headache, upper and lower back pain, shoulder pain, brassiere strap grooving, and rashes under the breasts. The psychosocial consequences are depression, anxiety, low self-esteem and dissatisfaction with body image, as well as difficulties in intimate relations and in participating in sports or social activities due to embarrassment. However, the scientific evidence of the effects of reduction mammoplasty has been weak or lacking. A meta-analysis reviewing the medical literature from 1985 to 1999 failed to recognise any prospective randomised studies (Chadbourne et al. 2001). Most of the studies were retrospective and the few prospective studies had methodological limitations. The paucity of solid scientific evidence raised the obvious need for prospective randomised studies (Iwuagwu et al. 2004), but practical and ethical considerations were thought to make this kind of study design impossible (Collins et al. 2002, Iwuagwu et al. 2004).

Patients' satisfaction with reduction mammoplasty has been previously studied at Helsinki University Central Hospital (Tykkä et al. 2001). In the present study the primary aim was to assess the effects of reduction mammoplasty. A comparison of the health burden (loss of quality of life) of symptomatic breast hypertrophy (in terms of general quality of life) with the general population and other surgical patient populations was carried out. This is required in order to identify and establish the value of reduction mammoplasty with respect to other surgical treatments. A search for factors affecting the outcome of reduction mammoplasty was also undertaken. Finally, an analysis of two to five years' (medium-term) follow-up data of reduction mammoplasty was carried out.

At the time when the present study was being designed and conducted, the formulation of the uniform criteria for access to non-emergency treatment in Finland was on the way. The act eventually came into force on 1 March 2005 (Finnish Ministry of Social Affairs and Health 2005), when this study was halfway through and all patients received their treatment within a reasonable time whether they participated in the study or not. Therefore, it was possible to design a randomised clinical trial with a six-month follow-up for the assessment of the short-term results. In order to achieve a comprehensive picture of the results, five questionnaires measuring different aspects of the effects of reduction mammoplasty were applied. We used two quality of life instruments complementing each other, as recommended in the literature (Hawthorne et al. 2001). As a condition-specific element, breast-related symptoms were evaluated. Pain is a central symptom and was therefore approached separately. The psychological aspects of reduction mammoplasty are another important area of consideration and they were also assessed separately. The medium-term results in terms of quality of life as well as breast-related and psychological symptoms were collected from the same prospective study population by post at two to five years' follow-up.

5 REVIEW OF THE LITERATURE

5.1 Definition of symptomatic breast hypertrophy and patient selection for surgery

Symptomatic breast hypertrophy has been described as chronic pain symptoms in at least three certain anatomic areas (head, neck, shoulder, bra groove, back or breast) in the upper body (Gonzalez et al. 1993b). Breast hypertrophy itself can be defined as the top 10th percentile in breast size of the female population (in the U.S. at least 750 cc or bra cup D) (Kerrigan et al. 2002). Definitions of cosmetic and reconstructive surgery were adopted by the American Medical Association in 1989 (American Society of Plastic Surgeons 2002). According to these definitions “reconstructive surgery is performed on abnormal structures of the body, caused by congenital defects, developmental abnormalities, trauma, infection, tumours or disease. It is generally performed to improve function, but may also be done to approximate a normal appearance.” In contrast “cosmetic surgery is performed to reshape normal structures of the body in order to improve the patient’s appearance and self-esteem.” The guidelines of reconstructive plastic surgery can also be applied to symptomatic hypertrophic breasts. Recently symptomatic breast hypertrophy has been stated to include a large variety of symptoms (Sigurdson et al. 2007a, Sigurdson et al. 2007b, Klassen et al. 2009, Pusic et al. 2009). Instruments specifically designed for symptomatic breast hypertrophy measure physical, psychosocial and sexual well-being.

Attempts at creating predictive objective models for successful surgery in breast hypertrophy (based on weight, height, body area or reduction specimen weight) have failed (Schnur et al. 1991, Miller et al. 1995, Seitchik 1995). On the contrary, the improvement in symptoms after surgery is independent of bra cup size, the weight of resection, height, weight, or body mass index (Gonzalez et al. 1993b, Collins et al. 2002). Patients with smaller resection weights per breast have an equal improvement in breast-related symptoms as those with greater resections (Spector and Karp 2007, Thoma et al. 2007). Only an increasing number of comorbid conditions have had a negative impact on the results (Collins et al. 2002). Previous studies have also noted a link between postoperative patient dissatisfaction and patient anxiety and/or depression, as well as the quality of the preoperative information, and patient-surgeon relations (Cerovac et al. 2005, Chahraoui et al. 2006).

Strömbeck and Malm introduced a priority grouping model for breast hypertrophy (Strombeck and Malm 1986). However, the model was more or less based on subjective, though clinically practical factors. The model was subsequently evaluated and it was concluded that it is an useful tool for selecting and priority grouping patients (Blomqvist 1996). It was certainly demonstrated that the tool worked in the way it was designed and it was widely used. However, the design of the system was not fully justified, but further modified on a somewhat subjective basis. The statement that this system is a useful tool for selecting patients and classifying priorities rouses up disagreement, because it has not been demonstrated that the outcome gain is related to the system itself.

Similarly, a height to sternal-notch-to-nipple ratio of less than five has been proposed as an “objective” discriminating criterion for reduction mammoplasty (Nicoletti et al. 2009). This ratio was obtained and applied into practice from retrospective reduction mammoplasty data and did not solve the problem of selecting patients for reduction mammoplasty.

At the moment the medical need for breast reduction surgery is still better defined by self-reports of symptoms rather than by the degree of breast hypertrophy present or the amount of breast removed (American Society of Plastic Surgeons 2002, Kerrigan et al. 2002). Recently designed instruments specifically for symptomatic breast hypertrophy may introduce new aspects in selecting patients. The content of these instruments have been derived from qualitative patient interviews (Sigurdson et al. 2007a, Sigurdson et al. 2007b, Klassen et al. 2009, Pusic et al. 2009). These strictly validated instruments may later be appropriate for patient selection by comparing the symptom levels found to those among the general population.

5.2 Outcomes in reduction mammoplasty

5.2.1 Assessing outcomes in reduction mammoplasty

An ideal outcome measure should be designed and developed specifically for a patient subgroup (Pusic et al. 2007a). It should be reliable (able to demonstrate consistent and reproducible scores), valid (able to measure what it is intended to measure), and responsive (sensitive to change).

In breast reduction surgery, symptom-based questionnaires have been traditionally used. During the last ten years, quality of life measurement has gained more interest, in addition to issues related to body image and self-esteem as well as the evaluation of psychosocial symptoms. Numerous outcome instruments have been used to assess aesthetic and reconstructive breast surgery (Ching et al. 2003, Pusic et al. 2007a). However, validated condition-specific instruments for symptomatic breast hypertrophy have been lacking (Pusic et al. 2007a). Until recently, only one breast reduction surgery instrument (Breast-Related Symptoms Questionnaire, BRSQ) (Kerrigan et al. 2001, Collins et al. 2002), has demonstrated acceptable development and validation. However, it has some content validity limitations. Therefore other instruments, such as quality of life and body image questionnaires have been used to complement the BRSQ outcome measure. For that reason, new outcome instruments containing items and domains covering physical, psychosocial and sexual well-being as well as patient satisfaction with the breast, outcome and care have been developed and validated (Sigurdson et al. 2007a, Sigurdson et al. 2007b, Klassen et al. 2009, Pusic et al. 2009). These instruments have items collected qualitatively through patient interviews therefore representing the true perspective of symptomatic breast hypertrophy. However, clinical studies applying these new instruments are yet to be conducted.

When choosing an outcome measure, a selection between or a combination of generic and condition-specific outcome measure should be made (Pusic et al. , Cano et al. 2009). A generic (quality of life) outcome measure has the advantage of

providing a tool for comparing different conditions and treatments with others or the general population. Nevertheless, it may not offer sufficient content validity or responsiveness to assess the effects of an intervention. On the other hand, a condition-specific outcome measure covers the area of interest studied more precisely and is therefore supposed to have better content validity and responsiveness. A recommendation of complementing a generic quality of life outcome measure with another one has been presented (Hawthorne et al. 2001). Overall, measuring general quality of life includes physical, social and mental well-being. The assessment of condition-specific quality of life adds important aspects or dimensions. In reduction mammoplasty, for instance, this means the evaluation of satisfaction with breast shape, size and symmetry, in addition to scars, the nipple-areola complex position and sensitivity among other things. These items and their importance are derived from patients, health professionals and the literature. Further formation of the outcome instrument is done by rigorous validation work as described recently in breast reduction surgery (Pusic et al. 2007b, Sigurdson et al. 2007a). The so-called Patient-Reported Outcome Measures (PROMs) are essential in assessing quality of life and patient satisfaction in surgery (Chow et al. 2009, Pusic et al. 2010).

5.2.2 Systematic reviews

A systematic review and meta-analysis of the published studies from 1985 to 1999 concluded improved clinical outcomes after reduction mammoplasty (Chadbourne et al. 2001). Twenty-nine out of the potential 131 studies met the eligibility criteria for meta-analysis. Most of the investigations were retrospective in design. A few prospective studies, but no prospective randomised controlled trials (RCTs) were found. The symptoms found to be improved were shoulder pain, shoulder (brassiere strap) grooving, upper and lower back pain, neck pain, rashes under the breasts, breast pain, headache, and pain or numbness of the hands. Physical functioning in health-related quality of life was also improved. However, the changes in psychological functioning were not statistically significant. A study reviewing the literature from 1966 to 1997 found a consistent improvement in physical symptoms and quality of life and a high degree of patient satisfaction (Jones and Bain 2001). Some improvement in body image and psychological well-being was also noted. However, the authors concluded that the criteria for meta-analysis were not fulfilled. In another review comparing outcome data for five classical and commonly used reduction mammoplasty techniques, a high rate of both physical and psychological improvement was reported (Daane and Rockwell 1999).

5.2.3 Prospective studies

After an era of retrospective studies mostly describing different techniques in reduction mammoplasty, a significant number of prospective studies have been published during the last 20 years (Hollyman et al. 1986, Gonzalez et al. 1993b, Hughes and Mahoney 1993, Cole et al. 1994, Klassen et al. 1996a, Klassen et al.

1996b, Shakespeare and Cole 1997, Starley et al. 1998, Giovanoli et al. 1999, Shakespeare and Postle 1999, Souza Faria et al. 1999, Behmand et al. 2000, Blomqvist et al. 2000, Chao et al. 2002, Collins et al. 2002, Harbo et al. 2003, Sood et al. 2003, Blomqvist and Brandberg 2004, Freire et al. 2004, Miller et al. 2005, Chahraoui et al. 2006, O'Blenes et al. 2006, Spector et al. 2006, Borkenhagen et al. 2007, Moskovitz et al. 2007, Spector and Karp 2007, Thoma et al. 2007, Eggert et al. 2009, Mello et al. 2009, Rogliani et al. 2009, Adham et al. 2010, Tykkä et al. 2010). However, some methodological drawbacks have affected the quality of these prospective outcome studies. When criteria for high-quality outcome assessment are applied – as regards validated outcome instruments or measures, adequate population size (minimum of 30 patients) as well as acceptable follow-up time (min. 6 months) and rate (about 3/4 or more) – a substantial number of studies still remain to be considered (Shakespeare and Cole 1997, Behmand et al. 2000, Blomqvist et al. 2000, Chao et al. 2002, Collins et al. 2002, Blomqvist and Brandberg 2004, Freire et al. 2004, Miller et al. 2005, O'Blenes et al. 2006, Borkenhagen et al. 2007, Thoma et al. 2007, Rogliani et al. 2009, Tykkä et al. 2010) (Table 1). In these studies improvement has been detected in quality of life, breast-associated symptoms, pain, muscle strength and posture, lumbar spine disability, psychological distress, self-esteem and body image as well as pulmonary function.

Rogliani et al. (2009) assessed 116 patients after 12 months. Four patients were lost to follow-up. A quality of life (SF-36) questionnaire, a condition-specific Symptom Inventory Questionnaire (SIQ), and a Body Dysmorphic Disorder Examination Self-Report (BDDE-SR23) questionnaire were used to measure outcome. All showed significant improvement.

Thoma et al. (2007) included 52 consecutive patients in their study. Their follow-up time was 12 months. At this point, however 19 patients (37%) were lost to follow-up. At six months follow-up, eight (15%) patients were lost. The instruments used were three quality of life questionnaires (Health Utilities Index Mark 2; HUI2, Health Utilities Index Mark 3; HUI3, and Short Form 36; SF-36), a condition-specific Breast Related Symptom Questionnaire (BRSQ) to measure breast-related symptoms, and the Multidimensional Body Self Relations Questionnaire (MBSRQ) to assess body image. At six months' follow-up, there was a significant reduction in pain and breast-related symptoms, improvement in the physical and mental summary scores of SF-36, and improvement in body image.

Behmand et al. (2000) had 69 patients followed-up for nine months. As outcome instruments they used the Short Form 36 (SF-36) to assess quality of life and the Brief Symptom Inventory (BSI) to assess psychological symptoms. Preoperatively, they found inferior quality of life and more psychological symptoms among the patients when compared to the general population. Postoperatively there was a statistically significant improvement in all measures.

Miller et al. (2005) enrolled 56 patients to their prospective study. The Short Form 36 (SF-36) quality of life questionnaire, the Symptoms Inventory Questionnaire (SIQ) for breast-related symptoms, and the Rosenberg Self-Esteem Scale (RSES) were applied for outcome analysis. All showed significant improvement at six months' follow-up. In addition, several quality of life scores were inferior to those of the general population preoperatively, and these were normalised postoperatively.

Chao et al. (2002) focused on lumbar spine disability (North American Spine Society Lumbar Spine Outcome Assessment Instrument), muscle strength (Kendall's muscle grading scale), posture (Harrison's objective clinical measurements) and pain (Visual Analogue Scale) when assessing women before reduction mammoplasty and at six months' follow-up. Fifty-five patients showed significant improvement in all measures. Although not using a specific instrument measuring breast reduction benefits, this study introduced an interesting viewpoint.

Shakespeare and Cole (1997) enrolled 110 patients to their prospective study and received follow-up data from 84 (76%) patients at six months. The Short Form 36 (SF-36) quality of life questionnaire and Rosenberg Self-Esteem Scale (RSES) were used as outcome measures. Both showed significant improvement from the preoperative to the postoperative state. The preoperative quality of life values inferior to those of the general population were normalised postoperatively.

Blomqvist et al. (2000) assessed 38 (78%) out of 49 patients at 12 months' follow-up. In addition to the Short Form 36 (SF-36) quality of life questionnaire, they assessed pain and discomfort symptoms. Quality of life and pain improved significantly after the operation. At three years' follow-up with the same population, the results were found to have remained stable (Blomqvist and Brandberg 2004).

Freire et al. (2004) evaluated quality of life with the Short Form 36 (SF-36) questionnaire preoperatively in 44 patients. Forty (91%) patients attended the six-month follow-up. However, smokers as well as those with chronic diseases, regular medication or body mass index over 30, or those who had breast-fed recently, were excluded from study. Nevertheless, the authors found a significant improvement in all areas of quality of life.

Borkenhagen et al. (2007) followed 40 consecutive patients for 6 months. Thirty-four patients (85%) completed the study. Several German standardised questionnaires were used to assess health-related quality of life (WHO Quality of Life Assessment, WHOQOL-BREF, 26 items), physical symptoms and complaints (Gießener Beschwerdebogen; GBB, 24-item scale version), psychological well-being (Berliner Stimmungsfragebogen; BSE, 6-scale version per 5 items), and life or global satisfaction (Lebenzufriedenheitsinventar; LZI, 15 items, and Anamnestic Comparative Self Assessment, ACSA, 1 item). A significant improvement was detected in psychological well-being and muscle complaints. However, physical well-being improved but the difference was not statistically significant. Increased euphoria was detected at six months' follow-up whereas other mood or affect characteristics improved but were not statistically significant.

In the original study by Collins et al. (2002) a total of 243 patients undergoing reduction mammoplasty were included. A set of standardised and validated instruments was used to assess outcome: the Short Form 36 (SF-36) and the European Quality of Life (EuroQol) for quality of life, the Multidimensional Body Self Relations Questionnaire (MBSRQ) for body image, Breast-Related Symptoms Questionnaire (BRSQ) for specific breast symptoms, and McGill Pain Questionnaire (MPQ) for pain. Control subjects, with hypertrophy controls (n = 88) and normal controls (n = 96), were also included in the study. At follow-up (mean 8.2, range 5.6–20.9 months) 179 patients (74%) were assessed. All measures, except for the fitness orientation of MBSRQ, showed statistically significant change from the preoperative to the postoperative situation. Postoperatively, the patients still reported higher pain levels than normal controls. Subjects with more co-morbidities gained less postoperative improvement.

O'Blenes et al. (2006) prospectively followed 68 patients and collected postoperative information at six and 21.5 months. The surveys were mailed. Breast-related symptoms, quality of life (SF-36) and the Rosenberg self-esteem questionnaire were used as outcome measures. Fifty-seven (84%) patients returned the mid-term follow-up surveys. The alleviation in breast-related symptoms and restoration of self-esteem remained stable and significant at both follow-up points. Quality of life was also significantly improved, except for the role emotional (limitations in usual role activities due to emotional problems) and mental health summary scores. The results also indicated that reduction mammoplasty provides rather physical than emotional improvement. However, some decrease in quality of life from the short-term to the long-term follow-up was noted. This was explained by a possible euphoria effect shortly after surgery.

As part of a larger prospective trial assessing health-related quality of life, Tykkä et al. (2010) followed 89 patients for six months. Eighty patients (90%) returned the six-month questionnaire. A significant improvement in overall quality of life (15D index score) was detected after reduction mammoplasty. Discomfort and symptoms showed the most improvement out of the dimensions of the 15D questionnaire.

Table 1. Prospective studies of reduction mammoplasty with valid outcome measures and an acceptable patient population size, follow-up time and follow-up rate.

| Author | Number of patients | Mean age (range) | Mean BMI | Resection per breast, mean (g) | Outcome measures | Follow-up in months, mean (range) | Follow-up rate |
|------------------------------|--------------------|------------------|----------|--------------------------------|------------------------------------|-----------------------------------|----------------|
| Tykkä et al. 2010 | 89 | 45 (18-73) | 26.7 | 607 | 15D | 6 | 90% |
| Rogliani et al. 2009 | 116 | 45 (19-65) | 26.5 | 500 | BRSQ, SF-36, BDDE-SR | 12 | 97% |
| Thoma et al. 2007 | 52 | 38 (20-68) | 30.9 | 790 | HUI-2, HUI-3, SF-36, BRSQ, MBSRQ | 6 | 85% |
| Borkenhagen et al. 2007 | 40 | 41 (17-67) | NA | NA | WHOQOL-BREF, GBB, BSE, LZI, ACSA | 6 | 85% |
| O'Blenes et al. 2006 | 68 | 39 (21-61) | 26.2 | 731 | BRSQ, SF-36, RSES | 22 | 84% |
| Miller et al. 2005 | 56 | 39 (21-61) | 26.6 | NA | BRSQ, SF-36, RSES | 6 | 100% |
| Freire et al. 2004 | 44 | 33 (18-59) | NA | 504 | SF-36 | 6 | 91% |
| Blomqvist and Brandberg 2004 | 49 | 39 (20-71) | 24.4 | 526 | SF-36 | 36 | 80% |
| Collins et al. 2002 | 243 | 39* | 29.7* | 814* | BRSQ, SF-36, EuroQol, MBSRQ, MPQ | 8 (6-21) | 74% |
| Chao et al. 2002 | 55 | 38 | 26.3 | 815 | NASS-LSOAI, Kendall, Harrison, VAS | 6 | 100% |
| Blomqvist et al. 2000 | 49 | 39 (20-71) | 24.4 | 526 | SF-36 | 12 | 78% |
| Behmand et al. 2000 | 69 | 36 (18-58) | NA | 837 | SF-36, BSI | 9 | 100% |
| Shakespeare and Cole 1997 | 110 | 35 (15-68) | 25.8 | NA | SF-36, RSES | 6 | 76% |

15D, 15D quality of life questionnaire; BRSQ, Breast-Related Symptoms Questionnaire; SF-36, SF-36 quality of life questionnaire; BDDE-SR, Body Dysmorphic Disorder Examination Self-Report; HUI2, Health Utilities Index Mark 2; HUI3, Health Utilities Index Mark 3; MBSRQ, Multidimensional Body Self Relations Questionnaire; WHOQOL-BREF, WHO Quality of Life Assessment; Anamnestic Comparative Self Assessment, ACSA; RSES, Rosenberg Self-Esteem Scale; EuroQol, EuroQol quality of life questionnaire, MPQ, McGill Pain Questionnaire; NASS-LSOAI, North American Spine Society Lumbar Spine Outcome Assessment Instrument; Kendall, Kendall's muscle grading scale; Harrison, Harrison's objective clinical measurements of spine movement; VAS, visual analogue scale; BSI, Brief Symptom Inventory, *for patients who attended follow-up. BMI, body mass index. NA, not available.

5.2.4 Randomised studies

A prospective randomised clinical trial (RCT) provides the strongest scientific evidence of a medical intervention. Ideally, it is blinded, preferably double-blinded – i.e., neither the patient nor the observer is aware of the treatment allocation. However, in visible plastic surgery, such as with reduction mammoplasty, blinding is impossible. Two randomised trials have been conducted during the recent years (Iwuagwu et al. 2005, Iwuagwu et al. 2006c, Iwuagwu et al. 2006d, Iwuagwu et al. 2006e, Freire et al. 2007, Neto et al. 2008). In these studies breast reduction has had a significantly positive impact on quality of life (Iwuagwu et al. 2006e), functional capacity and pain (Freire et al. 2007, Neto et al. 2008), depression and anxiety (Iwuagwu et al. 2006d, Iwuagwu et al. 2006e), self-esteem (Neto et al. 2008), and psychosocial aspects (Iwuagwu et al. 2006e). However, changes in lung function are less clear (Iwuagwu et al. 2006c), although patients with a greater resection seem to gain more from the procedure in terms of work of their breathing. While patients with macromastia seem to have an increased tendency to carpal tunnel syndrome (Iwuagwu et al. 2006a), an effect of breast reduction on nerve conduction to the upper limbs has not been noted (Iwuagwu et al. 2005).

In their prospective randomised clinical trial, Iwuagwu et al. (2006c, 2006d, 2006e and 2005) randomly allocated the patients either to have reduction mammoplasty within six weeks of the first examination or a delayed operation within six months of recruitment. The outcome measures included quality of life, psychological and psychosocial factors, lung function tests and upper-limb nerve conduction tests. The trial consisted of 73 patients, 36 of whom were assigned to have early and 37 delayed surgery. In two of the studies assessing quality of life, as well as psychological and psychosocial factors, all patients completed the study (Iwuagwu et al. 2006d, Iwuagwu et al. 2006e). In the study assessing lung function, eight patients were lost to follow-up, four in both groups (Iwuagwu et al. 2006c). The recruitment period in the study assessing nerve conduction of the upper limbs was only nine months in comparison to the 20 months of the other three studies, and therefore only 31 patients (16 to early, and 15 delayed intervention) were randomised (Iwuagwu et al. 2005). The follow-up time was three to four months. In their studies Iwuagwu et al. found that reduction mammoplasty significantly improved quality of life and emotional stability, and reduced the amount of depression and anxiety. No statistically significant effect was noted on lung function or nerve conduction of the upper limbs.

In the second RCT, 100 patients were randomly allocated to have immediate surgery (50 patients) or follow-up (Freire et al. 2007, Neto et al. 2008). The recruitment period coincided with that of the RCT of Iwuagwu et al. The follow-up time was six months. The outcome measures included functional capacity, pain and self-esteem. Freire et al. (2007) and Neto et al. (2008) found that reduction mammoplasty significantly improved functional capacity and self-esteem, and relieved pain in the lower back, shoulders and neck. However, smokers, patients with chronic diseases or regular medication as well as those with a body mass index over 30 or who had breast-fed recently were excluded from the study.

5.2.5 Medium and long-term results

Only a few medium-term prospective follow-up studies of reduction mammoplasty have been published. In a qualitative study the effects of breast reduction seem to remain stable at two years' follow-up (Shakespeare and Postle 1999). In two studies utilising standardised and validated instruments the effects of reduction mammoplasty stays stable and clinically substantial at two to three years' follow-up (Blomqvist and Brandberg 2004, O'Blenes et al. 2006). During the first months, a "honeymoon effect" can be detected, with stabilised results still comparable to population norms occurring later on (Blomqvist and Brandberg 2004, O'Blenes et al. 2006). Blomqvist et al. (2004) reported a small non-significant increase in patient-reported pain, especially headaches, from one to three years' follow-up. They concluded these changes to be connected to other factors than breast problems. However, a similar trend was also noted in patient-reported problems related to breast size and weight. Prospective long-term studies cannot be found in the literature.

5.2.6 Quality-adjusted life years and cost-utility of reduction mammoplasty

The gain in quality-adjusted life after reduction mammoplasty is approximately five years (Thoma et al. 2007). In other words, after breast reduction patients get to live in perfect health for several extra years, when compared to the alternative of dying immediately. This gain is cumulative during the additional life expectancy (approximately 30–40 years), but it gives a concrete example of the kind of impact an effective and early intervention has on quality of life. Others have suggested that conservative treatment attempts quickly exceed the costs of surgical treatment of symptomatic breast hypertrophy (Scholz et al. 2008).

Two studies (Taylor et al. 2004, Tykkä et al. 2010) have assessed the cost per quality-adjusted years (QALYs). In the most recent study (Tykkä et al. 2010), the QALYs gained after reduction mammoplasty were 0.930. With a 5% discount rate, the QALYs gained were 0.377. With a mean hospital cost of €3,383 of reduction mammoplasty, the mean cost per QALY was €3,638. With a 5% discount rate the cost per QALY was €8,973. In the other study (Taylor et al. 2004), the cost per QALY for breast reduction was approximately € 6,000–7,200. However, the Health-Related QoL data was obtained from a Swedish population, while the costs were derived from a British population.

In comparison to other interventions for other medical conditions, the cost per QALY obtained by breast reduction surgery is reasonable and indicates its cost-effectiveness. In Finnish studies using the 15D quality of life questionnaire, the cost per QALY has been found to be comparable to cervical or lumbar spine operations (anterior decompression of cervical spine [€2,770], or lumbar spine decompression to treat herniated disc or spondylosis [€1,740]) (Räsänen et al. 2006b), for hip arthroplasty (€6,710) or knee arthroplasty (€13,995) (Räsänen et al. 2007), cataract surgery (€7,947) (Räsänen et al. 2006a), or superficial venous surgery (€3,248) (Eskelinen et al. 2009).

5.2.7 Long-term sequelae of reduction mammoplasty

In Finland it has traditionally been recommended to women that they to have children before reduction mammoplasty to ensure successful breastfeeding. However, a recent review article found that women who have had reduction mammoplasty have an equal breastfeeding capacity when compared to women in the general population (Thibaudeau et al. 2010). Technically, it is important to preserve connections from the nipple-areola complex to a sufficient number of ducts and lobules. The majority of the reasons for breastfeeding difficulties are related psychosocial factors. Therefore, it is important to provide accurate information and encourage women to attempt breastfeeding even after reduction mammoplasty.

Advances in understanding the innervation anatomy have resulted in better understanding of how different techniques affect the sensation of the nipple-areola complex (Kuzbari and Schlenz 2007). Lateral, medial, inferior and central pedicles preserve the lateral and/or anterior cutaneous branches of the fourth intercostal nerve that is predominantly responsible for the nipple-areola complex sensitivity. In superior pedicle techniques these connections are cut. However, regardless of technique, sensitivity often improves after reduction mammoplasty, and this may be due to a release of a chronic traction injury to the nerve fibres in breast hypertrophy (Gonzalez et al. 1993a, Slezak and Dellon 1993). On the other hand, patients rarely complain about reduced sensitivity. Nevertheless, preserving the sensitivity and hence the sexuality of the nipple-areola complex should be considered as an important criterion in the selection of reduction mammoplasty technique (Thibaudeau et al. 2010).

Screening for breast cancer does not seem to be affected by reduction mammoplasty (Muir et al. 2010). However, fat necrosis may cause a palpable mass or radiographic features suggesting breast cancer (Mandrekas et al. 1994, Miller et al. 1998). Breast reduction itself may diminish the risk of breast cancer (Brown et al. 1999a). A lower incidence of breast cancer after reduction mammoplasty is not explained by a different location of breast cancer or breast tissue density (Muir et al. 2010). However, it has been found that women who have had breast reduction have an overall decrease in most cancers when compared with women in the general population (Boice et al. 1997, Boice et al. 2000, Fryzek et al. 2006).

5.3 Breast dimension assessment

Publications on comprehensive breast dimension assessment are infrequent. The few that are available include measurements of aesthetically perfect breasts or a clinical application for determining the breast augmentation volume required (Penn 1955, Westreich 1997), descriptions of breast dimensions in women with a variety of breast morphologies (Smith et al. 1986), comparisons of women with normal-sized breasts and women who seek breast reduction (Brown et al. 1999b), and a development of a formula including key breast dimensions for volume determination in breast hypertrophy (Sigurdson and Kirkland 2006). Others have utilised breast dimensions to establish formulas for resection weight estimation in reduction mammoplasty (Sommer et al. 2002, Descamps et al. 2008).

5.4 Reduction mammoplasty techniques

5.4.1 History of reduction mammoplasty techniques

More than 100 reduction mammoplasty techniques have been described (Daane and Rockwell 1999). However, in contrast to inventing new ideas, old ones are rather found and refined (Hall-Findlay 2002a). The evolution from a simple glandular reduction to include also nipple transposition on a pedicle and glandular remodelling lasted to the early 1930s (Lalardrie and Mouly 1978). Although the Biesenberger technique (Biesenberger 1928) had a high incidence of skin and nipple necrosis due to wide undermining, it remained the most popular breast reduction technique until the 1960s (Daane and Rockwell 1999). The beginning of the era of modern breast reduction techniques was in the early 1960s when an extensive separation of skin and gland was discarded and the nipple was transposed on a dermoglandular pedicle (Strombeck 1960, Dufourmentel and Mouly 1961, Pitanguy 1962, Skoog 1963, Pitanguy 1967). Only breast reduction with free nipple transplantation has remained from the earlier years as a choice for extreme cases (Thorek 1945). Due to the numerous published reduction mammoplasty techniques, an exhaustive review is beyond the scope of this thesis. Therefore, an overview of the most commonly used techniques is presented below.

5.4.2 Classification of modern reduction mammoplasty techniques

A classification of modern reduction mammoplasty techniques can be based on produced scars and nipple transposition pedicle patterns (Andrades and Prado 2008). The pedicle can be superior, medial, inferior, lateral, central, bipediced (horizontal or vertical), or combined. The scars can include a classic inverted T, a scar with a shorter submammary portion (short T, L, or J), vertical, horizontal, or periareolar. The pedicle direction and scar type can be chosen independently (Hall-Findlay 2002a). Because the most visible disadvantage of breast reduction is the scars, a practical approach is to base the classification on the scar patterns. Within these, different pedicles can be used to transpose the nipple and this has an impact on how the shaping of the breast tissue takes place. The subsequent event of breast remodelling after the operation is dependent on the technique chosen. A vertical breast reduction has the ability to narrow the breast and increase breast projection, whereas a horizontal reduction tends to flatten and easily broaden the breast (Hall-Findlay 2002a).

5.4.3 Inverted T scar reduction mammoplasty

The inverted T scar reduction mammoplasty has been a widely applied scar pattern. Several authors have successfully utilised this scar pattern in horizontal bi-pediced (Strombeck 1960), vertical bi-pediced (McKissock 1972, McKissock 1976),

central (Hester et al. 1985, Hester and Cukic 1988), and inferior pedicle reduction mammoplasty (Ribeiro 1975, Courtiss and Goldwyn 1977, Robbins 1977, Georgiade et al. 1979, Reich 1979). Of these, the inferior dermoglandular pedicle has been most widely used. In this technique the circulation to pedicle comes from the lateral thoracic, intercostals and internal mammary arteries and is therefore very reliable. A thin layer of tissue should, however, be left over the pectoralis fascia to preserve these vessels and the accompanied neural structures. The technique can be applied to breasts of most sizes. In very large breasts or breasts with extreme ptosis, resection may not be adequate and, therefore, a free nipple graft is indicated. Lateral resection must be appropriate enough, but tissue must be preserved medially for cleavage. The inferior pedicle has been the most common technique applied for breast reduction (Iwuagwu et al. 2006b, Nelson et al. 2008, Okoro et al. 2008). However, the scars are extensive, and there is a tendency towards hypertrophic scarring in the inframammary portion. The breast shape can be somewhat box-shaped or flattened. During the remodelling, as the inferior gland descends and the nipple rotates upwards, a bottoming-out may result in an unsatisfactory aesthetic result (Hall-Findlay 2002a).

5.4.4 The short scar reduction mammoplasty

In order to shorten the extensive incisions produced by the inverted T reduction mammoplasty, short scar techniques (short T, L, or J) have also been developed (Marchac and de Olarte 1982, Marchac 1986, Regnault 1990, Chiari 2002). All these techniques rely on a superior dermoglandular pedicle. However, most of these techniques (L and J scar patterns) have somewhat complex designs and are therefore more difficult to learn and produce. The short T scar technique presented by Marchac (Marchac and de Olarte 1982, Marchac 1986) is less complicated and it carries the same principles as the Lejour vertical reduction mammoplasty (Lejour 1994, Bohmert and Gabka 1997, Lejour 1999a, Lejour 1999b) and its later modifications (Pallua and Ermisch 2003, Hofmann et al. 2007).

5.4.5 Vertical scar reduction mammoplasty with superior pedicle

Arie and Pitanguy separately first described reduction mammoplasty with a superior pedicle and a vertical scar for moderately hypertrophic breasts (Arie 1957, Pitanguy 1962, Pitanguy 1967). However, for larger resections, a conversion to an inverted T scar was required. Nevertheless, the first approach to superior pedicle mammoplasty was made as early as in the 1920s (Dartigues 1925, Schwarzmann 1930).

Lassus performed a vertical scar reduction mammoplasty with a superior pedicle in 1964, described it in 1970, and modified the procedure to its final form in the mid 1980s (Lassus 1970, Lassus 1987, Lassus 1996, Lassus 1999). In this technique, a central wedge resection is performed without skin undermining. The vertical scar length varies according to the areola-inframammary distance, keeping in mind that it should end 3–7 cm above the inframammary fold (depending on the

breast size), because in this technique the inframammary fold ascends postoperatively. The superior pedicle should not be lifted more than 9 cm to avoid nipple necrosis; in such cases an alternative technique should be considered. The pedicle is thinned to contain 0.5–1 cm of glandular tissue. The glandular tissue beneath the lifted pedicle is included in the en bloc resection. The final adjustment of shaping is done by additional resections planned in a sitting position after temporary skin closure. Liposuction is not used.

Lejour developed a modification of the technique by Lassus in the late 1980s and published it in 1990 (Lejour 1994, Bohmert and Gabka 1997, Lejour 1999a, Lejour 1999b). The technique includes three principles differing from the technique of Lassus: wide lower skin undermining to allow skin retraction and to permit shorter scars, overcorrection in order to promote improved results in the long term, and use of liposuction in shaping the breast and in reducing extra tissue sensitive to weight changes. Lejour starts the operation with liposuction. However, care is taken not to aspirate the medial and lateral pillars too soft in order to make suturing them together easier. After lateral incisions, a wide skin undermining is performed laterally, medially and inferiorly. The future periareolar area is left intact. A central resection is performed at the level of the third intercostal space, creating a lateral and medial pillar. The pedicle can be thinned to 2–3 cm. An upper central anchoring suture is placed to elevate the retroareolar tissue to the superior dissection space. This suture was originally placed lower in the gland, but Lejour later modified it to be placed at the level of the upper margin of the areola. The pillars are sutured together with three or four sutures of slowly absorbable material. The sutures are placed anteriorly, starting below the areola, and progressively taking deeper bites when moving downward. This produces the conical shape of the breast. The skin is evenly gathered to shorten the scar. For resections of more than 1000 g another technique is recommended, especially in obese and older patients.

5.4.6 Vertical scar reduction mammoplasty with medial pedicle

After an early experience with Lejour's vertical reduction mammoplasty, Hall-Findlay developed a simplified vertical reduction mammoplasty technique (Hall-Findlay 1999, Hall-Findlay 2002a, Hall-Findlay 2002b). The nipple-areola complex is based on a medial dermoglandular pedicle that is easier inset and has a more reliable circulation, especially in larger resections. The thicker non-undermined pedicle, along with the fact that the pectoralis fascia is not exposed during resection, leads also to better sensation. However, vascular and neural elements of the pedicle have later been demonstrated to be located just below the dermis (Le Roux et al. 2009), and de-epitelisation should therefore be performed with caution. The vertical scar ends two to six cm above the inframammary fold depending on the breast size. Skin undermining is done only inferiorly to the inframammary fold. Pectoralis fascia sutures are not normally used to inset the pedicle. The medial and lateral glandular pillars are sutured together at the midline and are responsible for shaping the breast. Liposuction is applied for possible lateral fullness infrequently. When compared to the Wise pattern inferior pedicle technique, the Hall-Findlay technique reduces scarring, requires a shorter operative time, and is not more difficult to learn (Serra et al. 2010). Overall, the breast shape

is better when compared to the inferior pedicle technique and it is retained in long-term follow-up. However, others have noted persistent inferior dog-ear or teardrop deformity, and/or lateral deviation of the nipple as well as axillary fullness, and have therefore modified the technique to address these issues (Chen et al. 2003, Chen et al. 2004).

5.4.7 Vertical reduction mammoplasty in large resections

More recently, several authors have applied vertical breast reduction even to large resections (Pallua and Ermisch 2003, Poell 2004, Lista and Ahmad 2006, Hofmann et al. 2007, Ahmad and Lista 2008, Amin et al. 2010, Serra et al. 2010). In order to achieve more tissue resection, Lista and Ahmad (Lista and Ahmad 2006) have modified the Hall-Findlay technique to extend the excision more deeply into the skin superiorly and laterally. They also maintain all the skin flaps at a thickness of 2.5 cm in contrast to Hall-Findlay. However, they also thin the medial pedicle when needed. The upper border of the nipple-areola complex is planned preoperatively at the level of the inframammary crease, as the nipple-areola complex tends to rise an average of 1 cm after the operation (Ahmad and Lista 2008). Others have also recommended fixation of the submammary fold in large resections (Hofmann et al. 2007). When the contractibility of the skin is not satisfactory, lateral extension of the wound in the submammary fold, accompanied with extra skin excision, is also recommended (Pallua and Ermisch 2003, Hofmann et al. 2007).

5.4.8 Other vertical scar reduction mammoplasty techniques

To reduce long scars created in inverted T inferior pedicle reduction mammoplasty and to provide a better long-lasting shape without pseudoptosis, a short scar periareolar inferior pedicle reduction mammoplasty (SPAIR) was introduced (Hammond 1999, Hammond 2002). In this technique, the skin envelope is tailored during the operation and the resulting scar is vertical in most cases. A strong gathering periareolar suture is used. In addition securing sutures to the pectoralis fascia are used to create and secure the breast shape.

Circumvertical reduction mammoplasty with a superomedial pedicle is an evolution of vertical reduction mammoplasty techniques (Spear and Howard 2003). It utilises the skin markings similar to SPAIR with a superomedial pedicle similar to Hall-Findlay. Other techniques using various pedicles with periareolar and vertical openings have also been introduced (Van Thienen 2002, Mottura 2003, Atiyeh et al. 2005).

A resection through a periareolar incision for reduction mammoplasty was presented in the late 1980s (Benelli 1990). The nipple-areola complex is situated on a superior dermoglandular flap that is fixed to the pectoralis fascia superiorly. Lateral and medial glandular flaps are created after the resection and sutured together with a full breast-lacing suture. A hyperconvex shape is common shortly after the operation. Skin and glandular undermining is minimised.

Another procedure utilises a centrally based pedicle (Goes 1996, Goes 2003). In this technique, periareolar de-epithelialised skin acts as a support to the breast shape. The inclusion of an absorbable mesh support over this circular dermal flap further adds support to the breast. The skin undermining is wide. Glandular resection is performed superiorly and inferiorly.

5.4.9 Reduction mammoplasty with the free nipple graft

In extreme cases the free nipple graft reduction mammoplasty can be applied for patients with large ptotic breasts with no pleasurable nipple sensation (Clarkson 1950, Thorek 1963, Oneal et al. 1991, Koger et al. 1994). Overall, patients with unreliable or unpredictable nipple-areolar blood circulation on a dermoglandular pedicle are candidates for free nipple reduction mammoplasty (Oneal et al. 1991, Ahmed and Kolhe 2000). However, the operation is contraindicated if breast-feeding is planned in the future. The operation can be performed faster, which increases safety in higher-risk patients. An inverted T scar pattern is used and the free nipple graft is placed on the preoperatively positioned and de-epithelialised area.

5.4.10 Liposuction reduction mammoplasty

Liposuction has been introduced as an alternative method to traditional excision reduction mammoplasty (Gray 1998, Matarasso 2000, Gray 2001, Matarasso 2002, Moskovitz et al. 2004, Moskovitz et al. 2007). It is useful in scar-prone populations with darker skin. Liposuction can successfully reduce the breast volume by up to 2 litres. However, ptosis correction cannot be achieved or controlled as in conventional reduction mammoplasty, although some centimetres of mastopexia effect is obtained (Moskovitz et al. 2007). The technique is ideal for patients who complain about breast size and/or weight with or without ptosis-related issues. Patients issuing only ptosis complaints are not candidates for liposuction reduction mammoplasty.

5.4.11 Complications

Reduction mammoplasty is commonly associated with minor complications, such as local wound healing problems, due to long wounds and extensive raw tissue surfaces. More serious complications are fortunately rare. Systemic complications include sepsis, deep venous and/or pulmonary embolism, and pneumonia. Major local complications include haematoma requiring evacuation with or without blood transfusion, extensive skin or nipple necrosis, and deep infection (often due to fat necrosis). More common minor complications include haemorrhage without the need of surgical treatment, superficial opening of the wounds, superficial infection, suture material fistulas, minor skin edge necrosis or epidermolysis.

The need for venous thromboembolism chemoprophylaxis is determined by procedure and patient-related risk factors (Young and Watson 2006). Preoperative antibiotic prophylaxis to prevent postoperative infections has been found effective and safe (Tejirian et al. 2006, Throckmorton et al. 2009).

An inevitable consequence of the operation is the scars. The length of scars depends on the technique applied, as discussed in the reduction mammoplasty techniques above. However, there are individual differences in scarring. Hypertrophy or widening of the scars can cause aesthetically unpleasant results. Although scar problems cannot be directly categorised as a complication, it is a common reason for patient dissatisfaction or concern (Sprole et al. 2007).

In a Finnish patient population (n = 273) complications were found to be frequent (Setälä et al. 2007). Although every other patient had a complication, most of them were minor. Systemic complications such as sepsis, deep venous thrombosis or pulmonary embolism were not encountered. However, four percent of the patients had a haematoma requiring evacuation. Superficial infections were the most common (26%) and a deep infection was treated in nine percent of the patients. Almost 1/5 of the patients had some degree of skin necrosis and nine percent required revision surgery because of wound opening or skin and/or fat necrosis. The most frequent (13%) subsequent operations were for scars and puckers or liposuction for minor irregularities.

Other studies have also presented complication rates of 15%–53% (Cunningham et al. 2005, Hofmann et al. 2007, Roehl et al. 2008, Cardenas-Camarena 2009, Henry et al. 2009, Shah et al. 2010). The developers of the various techniques have shown somewhat lower rates (Lassus 1996, Lejour 1999b, Hammond 2002). Intraoperative hypotension has been found to be associated with postoperative haematoma (Henry et al. 2009). Some have not found obesity to increase complication rates (Setälä et al. 2007, Roehl et al. 2008), while others have suggested a higher body mass index to be associated with poorer outcome (Platt et al. 2003, O'Grady et al. 2005, Villani et al. 2009, Shah et al. 2010).

A direct comparison of complications in different techniques is difficult because the selection of the technique depends on the amount of resected tissue, skin elasticity, patient age, co-morbidities and degree of ptosis. However, after an appropriate learning curve and technical adjustments, vertical scar techniques with various pedicles seem to be as safe as the traditional inferior pedicle technique (Beer et al. 2004, Poell 2004, Lista and Ahmad 2006, Spector et al. 2006, Hofmann et al. 2007, Spector and Karp 2007).

5.4.12 Current trends in reduction mammoplasty techniques

An inferior pedicle with the inverted T scar pattern is still the most used technique in the United States, Canada, the United Kingdom and Ireland where it is used in 2/3–3/4 of all cases (Iwuagwu et al. 2006b, Nelson et al. 2008, Okoro et al. 2008). However, vertical short scar techniques have gradually gained popularity, probably among the younger plastic surgeons, and constitute 1/10–1/4 of all procedures. In Canada the technique of Hall-Findlay is popular, whereas in Europe the modifications of the Lejour technique are common. In Finland probably 2/3 of the procedures are done with the inferior pedicle and inverted T scar, whereas in the remaining 1/3 a superior or superomedial pedicle is used mainly with a vertical

scar (Setälä et al. 2007). The inferior pedicle with an inverted T scar is more likely to be selected by a junior surgeon or when the resection exceeds 500 grams.

6 AIMS OF THE STUDY

In this thesis, the health burden of breast hypertrophy and the effects of reduction mammoplasty are studied.

The specific aims of the present study were:

1. To assess how reduction mammoplasty affects patients' health-related quality of life and physical symptoms in terms of breast-associated symptoms and pain.
2. To assess how reduction mammoplasty affects patients' psychological symptoms in terms of depression, anxiety and self-esteem.
3. To compare the health burden of symptomatic breast hypertrophy to the age-standardised general population.
4. To compare the loss of quality of life caused by symptomatic breast hypertrophy to patient populations with major joint arthrosis.
5. To compare the effects (in terms of quality of life) of reduction mammoplasty to patients who have undergone major joint replacement surgery.
6. To look for factors affecting the outcome of reduction mammoplasty.
7. To assess the medium-term (two to five years') results of reduction mammoplasty.

7 PATIENTS AND METHODS

7.1 Patients (Studies I–V)

In August 2004 approximately 300 female patients were on the waiting list for bilateral reduction mammoplasty in the Hospital District of Helsinki and Uusimaa, Finland. The patients were approached by information letters and were asked to participate in the study. This thesis comprises eighty-two patients that agreed to attend the first examination. The patients were randomised either to be operated on (40 patients) or to be followed up (42 patients). The patients were operated on by plastic surgeons or trainees at the Department of Plastic Surgery at Helsinki University Central Hospital or at the Department of Surgery at Hyvinkää Hospital. Twenty-nine patients in the operative group and 35 patients in the non-operative group attended the follow-up and were included in the final statistical analysis (Studies I–IV). The baseline quality of life information of all 82 patients was compared to the age-standardised general population (Study II). The quality of life data of the twenty-nine patients who were operated on were compared to age-standardised population norms at both baseline and follow-up and to major joint replacement patient populations (Study II). In order to identify factors affecting the outcome, the data of the 29 operated patients was analysed (Study IV). All patients of the randomised trial who were eventually operated on (73 patients) were assessed for the medium-term follow-up results (Study V).

7.2 Power analysis

As part of the study plan power analysis, based on expected changes in values of the quality of life questionnaire SF-36 (Collins et al. 2002), was carried out to determine adequate patient sample sizes for the prospective randomised study. Power ($1-\beta$) was set at 0.9 and $\alpha \leq 0.01$. As a result, a target of 45 patients and a minimum of 30 patients in both groups were considered sufficient. With a total number of 82 patients participating in the study, this aim was achieved.

7.3 Randomisation

In order to control possible confounding factors, patients' age, height, weight and mean breast volume [(right breast volume + left breast volume): 2] were entered into a file in a coded format. The patients were grouped and ordered within the groups by age, height, weight and mean breast volume, respectively. Cut-off points were derived from a basic analysis of the data (Table 2). Nineteen groups were formed with two to seven patients in each. Ten patients were left as singles not having a group match based on the stratification criteria mentioned above. After

this, stratified randomisation was applied to allocate patients to either the operative (A) or the non-operative group (B) by picking the combination AB or BA from a random seed list. From groups with odd numbers of patients, one patient (last in the group list) was left over. At this phase 64 patients were randomised and 18 patients were not. The remaining patients were randomised by the minimizing method. With this method, the best option for group balance was calculated and the patient was grouped (A or B) based on this value. If the situation was a draw, the grouping was made by picking the combination AB or BA from the random seed list and by using the first letter. The patients were randomised by means of the minimizing method in the previously set order (stratification), and each randomised patient was taken into account in the calculation for the following patient. By these two methods, 40 patients were randomised to the operative group (A) and 42 patients to the non-operative group (B).

Table 2. Factors and cut-off points used for stratified randomisation.

| Factor | Cut-off points | | | |
|------------------------|----------------|-------|-------|--------|
| Age (years) | < 35 | 35–45 | 45–55 | > 55 |
| Height (cm) | < 162 | | | > 162 |
| Weight (kg) | < 70 | 70–90 | | > 90 |
| Breast volume (litres) | < 1.35 | | | > 1.35 |

7.4 Questionnaires (Studies I–V)

Questionnaires measuring different aspects of the effects of reduction mammoplasty were used to reach an objective and a comprehensive picture of the results. Because none of the generic quality of life instruments available can be considered as a golden standard or superior to others, we wanted to clarify the results by using two quality of life instruments complementing each other, as recommended in the literature (Hawthorne et al. 2001). As a condition-specific element, breast-related symptoms were evaluated. Pain is a central symptom and was therefore approached separately. The psychological aspects of reduction mammoplasty were also assessed with a mood questionnaire.

7.4.1 SF-36 (Studies I and IV)

The Short Form-36 Health Survey (SF-36) is a validated and widely used questionnaire to assess health-related quality of life. It contains 36 items forming eight health subscales (physical function and activities, daily activities, emotional

status, social activities, mental health, vitality and energy, pain and general health), two summary scores (physical health and mental health), and a single health Utility Index Score (SF-6D) (Ware et al. 1993, 2000, Ware and Kosinski 2001). Higher scores represent better health. We used the Utility Index Score (SF-6D) to demonstrate the changes as a whole, but also the Physical and Mental Summary Scores to demonstrate changes separately for physical and mental functions. The SF-6D ranges from 0.29 to 1.00, and 0.033 is considered to be the minimal clinically important difference (Walters and Brazier 2003). The two summary scores represent a norm-based scoring with a mean value of 50 and a standard deviation of 10. Minimal clinically important differences have not been established for the summary scores. For this reason, we settled on using a half standard deviation as the minimal clinically important difference as suggested (Sloan et al. 2003).

7.4.2 15D (Studies I–II and IV–V)

15D is another generic and standardised questionnaire of health-related quality of life that also includes both profile and a single index score measures (Sintonen 2001). It consists of 15 dimensions: breathing, mental function, speech (communication), vision, mobility, usual activities, vitality, hearing, eating, elimination, sleeping, distress, discomfort and symptoms, sexual activity, and depression. For each dimension, the respondent must choose one of the five levels that best describes his/her state of health at the moment (the best level = 1; the worst level = 5). The valuation system of the 15D is based on an application of the multi-attribute utility theory. A set of utility or preference weights has been elicited from the general public through a 3-stage valuation procedure. These are used to generate the dimension level values and the overall utility score – i.e., the 15D score (single index number) over all the dimensions on a scale of 0–1. The maximum score is 1 (no problems on any dimension) and minimum score 0 (equal to being dead). The minimal clinically important difference in the 15D score is considered to be 0.03. The 15D quality of life questionnaire compares favourably with other similar instruments in most of the important properties (Sintonen 1995, Stavem 1999, Hawthorne et al. 2001, Sintonen 2001, Moock and Kohlmann 2008). 15D has been developed and widely used in Finland and was therefore chosen as the second quality of life instrument to be used in this study.

7.4.3 FBAS (Studies I and IV–V)

The Finnish Breast-Associated Symptoms (FBAS) questionnaire evaluates symptoms commonly associated with breast hypertrophy. The English version of the Breast-Related Symptoms Questionnaire (BRSQ) has been validated (Kerrigan et al. 2001). Our questionnaire is a modification of this questionnaire translated into Finnish. In the questionnaire, patients are asked 13 questions on subjects including upper back pain, difficulties in finding clothing, headaches, breast pain, lower back pain, intertrigo, painful brassiere strap grooves, difficulties in participating in sports, neck pain, shoulder pain, difficulties in running, pain or

numbness in the hands, and arm pain. The categorical choices for answers are “all of the time”, “most of the time”, “some of the time”, “a little of the time”, and “none of the time”. A single Breast-Associated Symptoms Score (with equal weights for all questions) ranging from zero to 100 was calculated for statistical evaluation. Higher scores indicate more symptoms.

7.4.4 FPQ (Studies I and IV)

The Finnish Pain Questionnaire (FPQ) contains word groups describing pain (Ketovuori and Pontinen 1981). The words have a quantified measure ranging from zero to 100 for statistical analysis. A change from one word to another within a group is considered clinically important. As a quantified measure, this change ranges from eight to 30 with a mean of 18 and was used as the minimal clinically important difference. Pain evaluation was specified to the upper body only. A single pain score (mean pain for a word group) was calculated for statistical analysis. Higher scores indicate more pain.

7.4.5 RBDI (Studies III–V)

The RBDI mood questionnaire (Raitasalo 2007) is Raitasalo’s modification of the short form of the Beck Depression Inventory (BDI) (Beck and Beck 1972, Beck et al. 1974), and has been used in Finland for nearly 30 years. It has 13 questions for depression and one for anxiety. Evaluation of self-esteem is included in all 14 questions. The depression score ranges from zero to 39 points. Five to seven points refer to mild depression, eight to fifteen points to moderate depression, and over sixteen points to severe depression. Anxiety has four categories (0 = none, 1 = mild, 2 = moderate, and 3 = severe anxiety). The self-esteem scores range from zero to fourteen points. Extremely high scores of self-esteem may indicate a manic condition.

The questionnaire is useful in measuring depression and self-esteem among adults, working people, the elderly, students, schoolchildren, those with psychosomatic symptoms, those in rehabilitation, and patients with major depressive disorders (Kaltiala-Heino et al. 1999, Hietanen et al. 2001, Raitasalo 2007). In the Finnish series the internal consistency of the depression scale ranges between 0.66 and 0.93, and of the self-esteem scale between 0.76 and 0.84. In the adult population, the depression scale correlates with the original Beck Depression Inventory at 0.88 in an unselected population and 0.90 among those with a major depressive disorder, and with the Hamilton Rating Scale for Depression (Ham-D) at 0.60 and 0.82, respectively (Raitasalo 2007).

7.5 Breast measurements (Studies I–IV)

All breast dimension measurements were taken in a normal standing position with the shoulders back and the head facing straight ahead. Breast volume was measured with plastic cup devices. Cup volumes ranged from 150 ml to 2,700 ml, with intervals from 30 ml to 200 ml correspondingly to increasing volume. When breast volume fell between the cup volumes, an estimate of the accurate volume was made (by visual partition of the interval into two to four divisions). The anthropometric measurements taken were chest circumference at the level of the inframammary crease and breast circumference at the level of the nipples, as well as the distance from the clavicle to the nipple, from the sternal notch to the nipple, from the nipple to the midline and from the nipple to the inframammary crease, in addition to the horizontal diameter of the areola. Measurements were taken from the upper border of the clavicle 5 cm lateral from the sternoclavicular joint and from and to the center of the nipple.

7.6 Statistical analysis (Studies I–V)

The data were analysed with the SPSS®. The basic scoring of SF-36 was made with SF Health Outcomes™ Scoring Software. The algorithm for the basic scoring of 15D ran on SPSS® was obtained from the developer of the instrument. Kolmogorov-Smirnov and Shapiro-Wilk tests were applied to screen normality and Levene's test to screen equality of variances.

In studies I–V, the independent-samples *t* test or paired *t* test was used for continuous variables meeting the assumption of normally distributed data. For data not meeting the assumption of normal distributions, or for categorical values, the Mann-Whitney U test or the Wilcoxon signed rank test was applied. The Chi square test or McNemar test was used to compare patient proportions. Fisher's exact test was applied when appropriate. Probabilities of less than 0.05 or less than 0.01 were accepted as significant, depending on the study setting. To control possible false positive findings due to multiple statistical testing, the Bonferroni correction was applied when needed.

In Study I, analysis of covariance (ANCOVA) was applied for instrumental comparison between the two patient groups. The F-test probability value for entering and removal was 0.05 and 0.1, respectively. The first examination value of a particular instrument was included in the model. According to the randomisation method, covariates (age, height, weight and mean breast volume) were tested for inclusion in the models. Sixty-four patients who completed the follow-up were included in the statistical analysis for comparison of the operative and non-operative group. The confidence level chosen was 95%. Probabilities of less than 0.01 were accepted as significant.

In Study II, an age-standardised comparison to the general female population was made for 82 patients at baseline and, for the operated 29 patients, separately at baseline and follow-up. Simple linear regression analysis was used to establish the mean difference in the 15D score from baseline to six months postoperatively between the groups of patients, adjusted for age and baseline 15D score. In this

way the operated 29 patients were also compared to those who had received a joint replacement. Probabilities of less than 0.05 were accepted as significant.

In Study III, the depression and anxiety categories were dichotomised by combining the mild, moderate and severe categories into a “symptomatic” category for statistical comparison. Probabilities of less than 0.05 were accepted as significant.

In Study IV, simple linear regression was applied to assess correlations between outcome measure changes and patient-related variables. A positive outcome measure change indicates a positive clinical outcome. The F-test probability value for entering and removal was 0.05 and 0.1, respectively. As a result of the Bonferroni correction for multiple statistical testing, a significance level of less than 0.006 was established as significant.

In Study V, comparison from baseline to follow-up was made for the 62 patients who returned the follow-up data. The depression and anxiety categories were dichotomised by combining the mild, moderate and severe categories into a “symptomatic” category for statistical comparison. Probabilities of less than 0.01 were accepted as significant. Age-standardised comparison to the general female population was made for these patients at follow-up. Probabilities of less than 0.05 were accepted as significant.

In order to estimate the internal responsiveness (i.e., sensitivity to change), effect size (ES) and standardized response mean (SRM) were calculated for each instrument (Thoma et al. 2005, Livingston et al. 2009). These estimates describe how good the used instruments were in detecting possible changes in our patient population. Effect size is calculated by the difference (Δ = mean follow-up score minus mean baseline score) divided by the standard deviation of the baseline scores. The standardized response mean (SRM) is the mean change scores divided by the standard deviation of the change scores. An effect size of less than 0.20 can be considered as insignificant, an effect size between 0.20 and 0.50 as small, an effect size between 0.50 and 0.80 as moderate, and an effect size greater than 0.80 as large (Cohen 1977).

8 ETHICS

Approval for the studies was obtained from the Surgical Ethical Research Committee of the Hospital District of Helsinki and Uusimaa. Patients were approached by means of information letters and they were asked to participate in the study. For Studies I–IV, possible patient questions were addressed over the telephone or at the fist examination. After agreement, patients signed an informed consent. For Study V, patients returned their consent along with the questionnaires by post. The study was conducted in accordance with the guidelines of the Declaration of Helsinki.

9 RESULTS

9.1 General results (Studies I–IV)

The characteristics of the whole patient population are presented in Table 3. Mean follow-up time for the operative and the non-operative (conservative) group was 6.5 months (range 5.8–7.8) and 6.2 months (range 6.1–6.5), respectively. One patient in the operated group and seven patients in the conservative group did not want to continue in the study. Ten operations were postponed for organisational reasons or the patients' preferences. As a result, 29 patients from the group operated on and 35 patients from the conservative group were followed. Withdrawals (eleven patients in the operated group and nine patients in the conservative group) did not differ significantly from the patients who completed the study (data not shown). Patients in the conservative group were operated shortly (2–10 months) after the follow-up examination.

After randomisation, 29 patients were operated on with a mean intervention delay of 4.1 months (range 1.9–6.7). The techniques used were Strömbeck (12 patients), superior pedicle with vertical scar (eight patients), inferior pedicle (eight patients), and free nipple graft (one patient). The mean weight of resection for the right and left breast was 655 g (range 200–1300) and 685 g (range 210–1360), respectively. Three patients had adjacent liposuction (total volume of 220, 80 and 20 ml, respectively). The mean hospitalisation time was 3 days (range 2–4). Prophylactic medication against venous thrombosis and infection was given to 14 and 22 patients, respectively.

Among 29 patients, there were one (3%) systemic complication (pulmonary embolism) and three (10%) major local complications (two haematoma evacuations and one nipple necrosis). Local wound healing problems were common (14 patients, 48%). Twelve (41%) patients suffered a superficial opening of the wound. Six of these patients required antibiotics for a short period. Four (14%) haematomas required no surgical intervention. Three (10%) “dog-ears” (puckers) required later treatment and one (3%) minor nipple necrosis was revised shortly after the primary operation.

9.2 General results (Study V)

Sixty-two patients (85%) agreed to participate in the long-term follow-up study and returned the follow-up data. These patients were included in the final statistical analysis. Non-responders did not differ from responders as regards baseline characteristics (data not shown). The mean follow-up time was 4.0 years (range 2.3–4.6). At the operation the mean age of the patients was 48.1 (Sd 10.4) years. The mean weight of resection for the right breast was 738 (Sd 398) grams and for the left breast 754 (Sd 375) grams.

Table 3. Studies I–IV. Patient population characteristics (n=82).

| | | |
|---|-----------------------------|--------------|
| Age (years), mean (Sd) | | 46.7 (1.0) |
| Height (m), mean (Sd) | | 1.63 (0.06) |
| Weight (kg), mean (Sd) | | 79.8 (12.6) |
| BMI (kg/m ²), mean (Sd) | | 30.1 (4.6) |
| Smoking, n (%) | | 18 (22) |
| Alcohol six or more doses per week, n (%) | | 12 (15) |
| Previous breast surgery, n (%) | | 9 (11) |
| Co-morbidities, n (%) | | 46 (56) |
| | Hypertension n (%) | 20 (22) |
| | Diabetes, n (%) | 1 (1) |
| | Asthma, n (%) | 15 (18) |
| | Autoimmune disease, n (%) | 6 (7) |
| | Psychiatric disease, n (%) | 11 (13) |
| Parturition, n (%) | | 61 (75) |
| Marital status | | |
| | Married, n (%) | 47 (57) |
| | Live-in relationship, n (%) | 12 (15) |
| | Divorced, n (%) | 7 (9) |
| | Widow, n (%) | 2 (2) |
| | Single, n (%) | 14 (17) |
| Education | | |
| | Elementary school, n (%) | 25 (31) |
| | Polytechnic, n (%) | 44 (54) |
| | University, n (%) | 13 (16) |
| Employed, n (%) | | 65 (79) |
| Work load physical | | |
| | office, n (%) | 35 (43) |
| | light, n (%) | 12 (15) |
| | moderate, n (%) | 33 (40) |
| | heavy, n (%) | 2 (2) |
| Right breast volume (litres), mean (Sd) | | 1.36 (0.38) |
| Left breast volume (litres), mean (Sd) | | 1.40 (0.39) |
| Chest circumference (cm), mean (Sd) | | 94.5 (8.9) |
| Breast circumference (cm), mean (Sd) | | 111.5 (10.0) |
| Clavicle to nipple Right (cm), mean (Sd) | | 34.7 (4.2) |
| Clavicle to nipple Left (cm), mean (Sd) | | 34.5 (4.0) |
| Sternal notch to nipple Right (cm), mean (Sd) | | 33.7 (4.1) |
| Sternal notch to nipple Left (cm), mean (Sd) | | 34.0 (3.9) |
| Nipple to inframammary crease Right (cm), mean (Sd) | | 15.5 (4.1) |
| Nipple to inframammary crease Left (cm), mean (Sd) | | 16.2 (4.0) |
| Nipple to midline Right (cm), mean (Sd) | | 12.4 (1.7) |
| Nipple to midline Left (cm), mean (Sd) | | 12.5 (1.8) |
| Areola horizontal diameter Right (cm), mean (Sd) | | 7.8 (2.0) |
| Areola horizontal diameter Left (cm), mean (Sd) | | 8.1 (1.8) |

Values are expressed as means with standard deviations (Sd) or, in categorical cases, as frequencies (n) with percentages (%). BMI, body mass index.

9.3 Effect sizes and standardized response means

With the exception of the mental summary score of the SF-36 quality of life questionnaire (effect size medium, i.e. 0.5-0.8), the effect sizes of the outcome measures were large (i.e., over 0.8) (Table 4).

Table 4. Effect sizes (ES) and standardized response means (SRM) for the outcome measures.

| Outcome measure | Change (Δ) | Sd (baseline) | Sd (Δ) | ES | SRM |
|-----------------------|---------------------|---------------|-----------------|------|------|
| SF-36 HRQoL | 0.174 | 0.133 | 0.136 | 1.31 | 1.28 |
| Physical health score | 9.73 | 8.70 | 6.814 | 1.12 | 1.43 |
| Mental health score | 7.80 | 11.24 | 11.24 | 0.69 | 0.69 |
| 15D HRQoL score | 0.086 | 0.083 | 0.063 | 1.04 | 1.37 |
| Breast symptoms | 47.94 | 14.97 | 14.45 | 3.20 | 3.32 |
| Pain | 21.43 | 14.71 | 17.22 | 1.46 | 1.24 |
| Depression | 3.38 | 3.96 | 2.91 | 0.85 | 1.16 |
| Self-esteem | 3 | 3.19 | 2.38 | 0.94 | 1.26 |

HRQoL, Health-Related Quality of Life; ES = Δ /Sd; SRM = Δ /Sd (Δ).

9.4 The effects of reduction mammoplasty on quality of life and physical symptoms (Study I)

For SF-6D and PCS, a statistically and clinically significant difference was found, with all the values within the confidence interval of difference being clinically important. The confidence interval of difference for the MCS was broader, with some of the values not being clinically important (Table 5).

The 15D index score yielded statistically and clinically significant differences between the operative and the non-operative group at the second examination. All values within the confidence interval of difference were also clinically important.

The 29 operated patients reported significantly fewer breast-associated symptoms or less pain when compared with the non-operated patients at the second examination. For pain, practically all the values within the confidence interval of difference could be considered clinically important.

Twenty-eight patients (97%) were overall satisfied with the surgical result and would have had the operation again. Twenty-one patients (72%) were satisfied with their breast size; six patients (21%) found them too large and two patients (7%) too small. Twenty-three patients (79%) were satisfied with the breast shape, and six (21%) were unsatisfied. Five of these patients rated their breasts still too large, whereas one patient thought her breasts were too small postoperatively.

Table 5. Reduction mammoplasty patients' outcome measure data at first and at second examinations.

| | Operative group 29 patients | Non- operative group 35 patients | <i>p</i> * (CID) |
|-----------------------------------|-----------------------------------|--|------------------------|
| SF-36 Utility Index Score (SF-6D) | | | |
| First examination | 0.645 (0.138) | 0.657 (0.131) | 0.734 (-0.079 ; 0.056) |
| Second examination | 0.820 (0.143) | 0.663 (0.136) | 0.0001 (0.107 ; 0.220) |
| SF-36 Physical Summary Score | | | |
| First examination | 42.0 (8.6) | 42.6 (8.9) | 0.770 (-5.0 ; 3.8) |
| Second examination | 51.7 (7.6) | 43.3 (7.8) | 0.0001 (5.8 ; 11.8) |
| SF-36 Mental Summary Score | | | |
| First examination | 46.0 (12.2) | 47.2 (10.5) | 0.672 (-6.9 ; 4.5) |
| Second examination | 53.8 (8.4) | 46.2 (13.1) | 0.002 (3.2 ; 13.1) |
| 15D Index Score | | | |
| First examination | 0.831 (0.090) | 0.855 (0.076) | 0.248 (-0.066 ; 0.017) |
| Second examination | 0.917 (0.075) | 0.861 (0.087) | 0.0001 (0.041 ; 0.103) |
| Breast-Associated Symptoms Score | | | |
| First examination | 59.7 (14.8) | 61.4 (15.3) | 0.658 (-9.2 ; 5.9) |
| Second examination | 11.8 (7.7) | 57.9 (14.3) | 0.0001 (-49.2 ; -40.7) |
| Pain Score | | | |
| First examination | 28.5 (16.6) | 27.5 (13.2) | 0.787 (-6.4 ; 8.5) |
| Second examination | 7.0 (8.4) | 26.5 (13.5) | 0.0001 (-25.2 ; -14.3) |

Values are mean (Sd). BMI, body mass index. SF-36, Short Form-36 quality of life questionnaire. 15D, 15D quality of life questionnaire. *ANCOVA, CID = 95% confidence interval of difference.

9.5 Comparison to the general population and patients undergoing major joint replacement surgery (Study II)

At baseline patients (n=82) showed significantly lower mean values for most of the dimensions, and lower mean 15D scores than the age-standardised general female population (Figure 1). The dimensions of discomfort and symptoms, distress, and vitality showed particularly low values. The extent of the health deficit (0.09) for symptomatic breast hypertrophy was well above the minimal clinically important difference of 0.03. A separate baseline comparison for the operated 29 patients demonstrated the same findings (Figure 2). Postoperatively, there was no difference in the mean 15D score between the operated 29 patients and the general population (Figure 3).

Figure 1. The 15D profiles of all patients (n=82) at baseline, compared to the age-standardised general female population (n=2532); * significantly worse HRQoL among the patients than in the general population at the $p < 0.05$ level, ** at the $p < 0.01$, and *** at the $p < 0.001$ level.

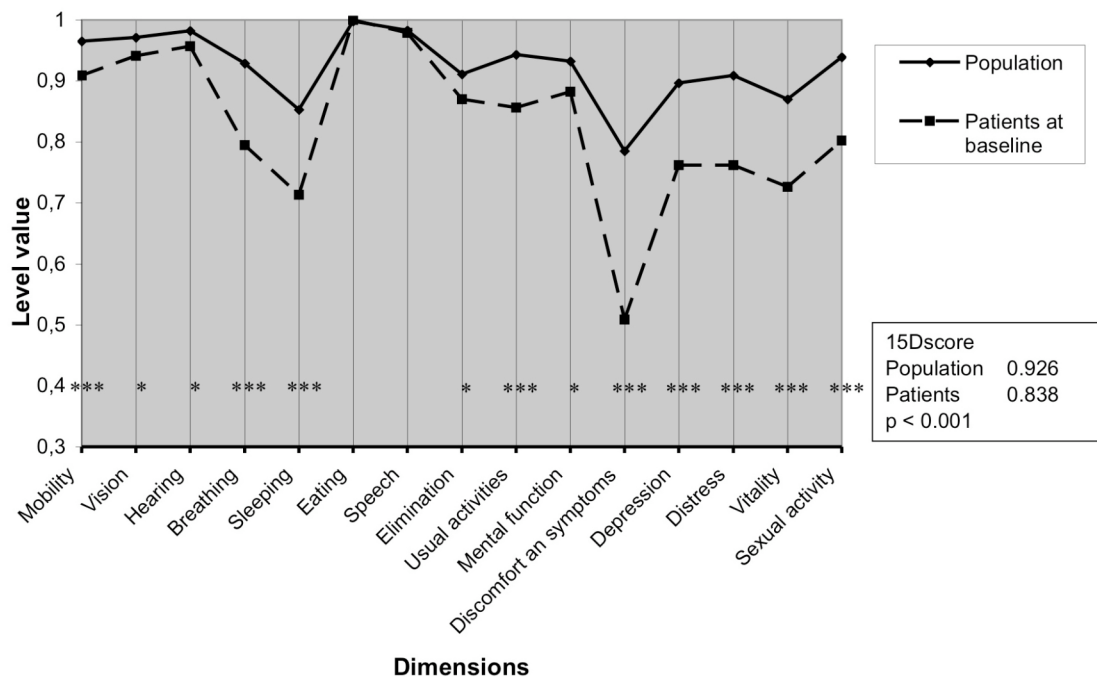


Figure 2. The 15D profiles of the operated patients (n=29) at baseline, compared to the age-standardised general female population (n=2497); * significantly worse HRQoL among the patients than the general population at the $p < 0.05$ level, ** at the $p < 0.01$, and *** at the $p < 0.001$ level.

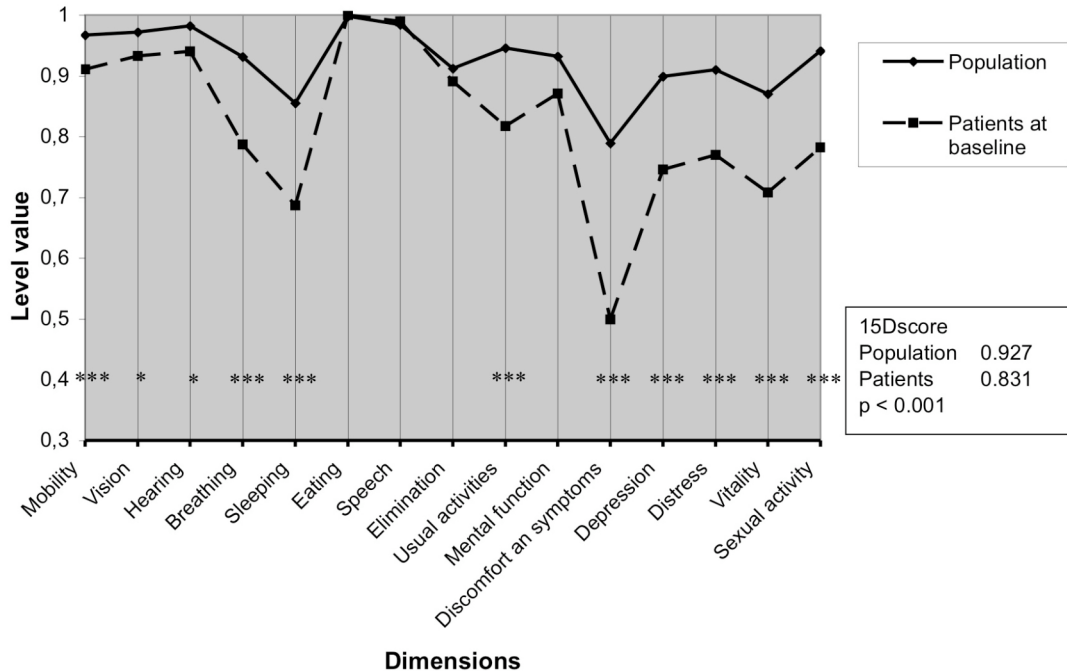
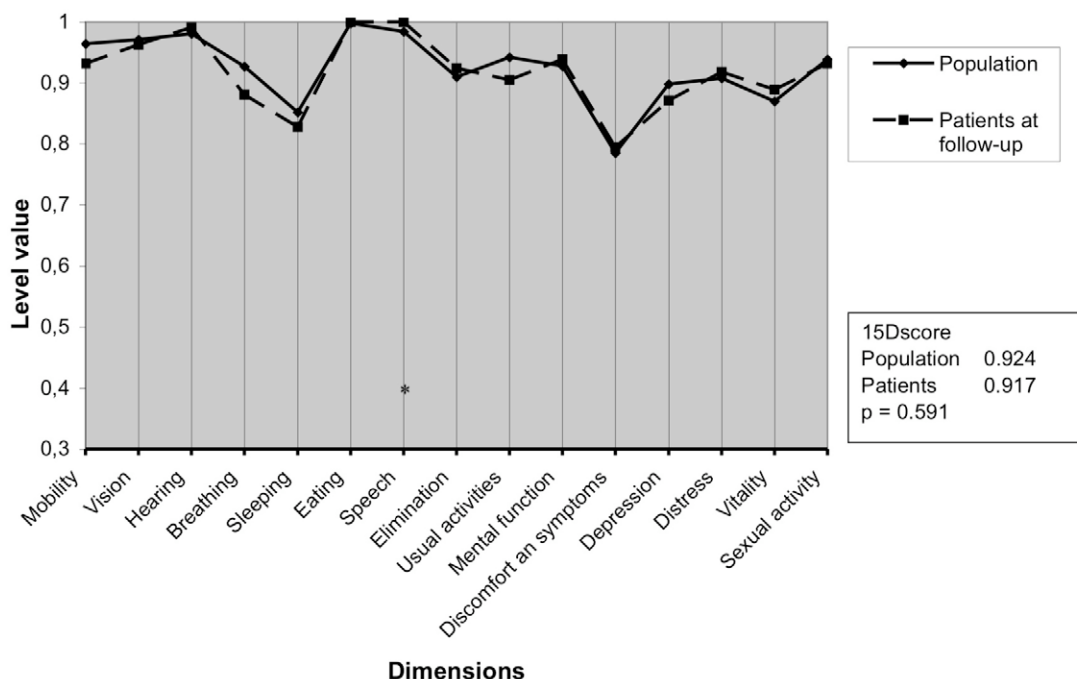


Figure 3. The 15D profiles of the operated patients (n=29) at follow-up, compared to the age-standardised general female population (n=2468); * significantly better HRQoL among the patients than the general population at the $p < 0.05$ level.



When compared preoperatively, patients who had undergone reduction mammoplasty (this study, n=82) and those who had undergone major joint replacement (Räsänen et al. 2007) showed no differences in the mean 15D score (adjusted for age with linear regression analysis). Postoperatively, both reduction mammoplasty (p = 0.03) and total hip replacement (p = 0.002) yielded a greater improvement in health-related QoL than total knee replacement (adjusted for age and baseline 15D score with regression analysis). The adjusted changes in the 15D score were 0.064 for reduction mammoplasty (n=29), 0.055 for total hip joint replacement (n=95) and 0.022 for total knee joint replacement (n=102). The intervention effect of reduction mammoplasty (0.064) was also well above the minimal clinically important difference of 0.03.

9.6 The effects of reduction mammoplasty on psychological symptoms (Study III)

At the first examination 33 patients (52%) were not depressed, and 16 patients (25%) suffered from mild, 14 from moderate (22%), and one from (2%) severe depression. Twenty-eight patients (44%) were not anxious, while 32 patients (50%) had mild, three patients (5%) moderate, and one patient (2%) severe anxiety. Overall, only 23 (36%) of the patients showed no signs of depression or anxiety at baseline. There were 9 (31%) and 14 (40%) asymptomatic patients in the operative and conservative group at baseline, respectively.

At the first examination the median depression score for the operated patients (n=29) was 5 (interquartile range 2.5–6.5) and the self-esteem score 3 (1.5–7.0). For the conservatively treated patients, the respective values were 4 (1.0–8.0) and 5 (2.0–7.0). The differences were not statistically significant ($p=0.63$ for depression and $p=0.22$ for self-esteem, Mann Whitney U test). At the second examination, patients in the operative group had significantly less depression ($p < 0.01$) and higher self-esteem ($p = 0.03$) when compared with the conservatively treated group. The median depression score postoperatively for the operated patients was 0 (interquartile range 0.0–2.5) and the self-esteem score 7 (5.5–10.0). For the conservatively treated patients, the respective values were 4 (0.0–7.0) and 5 (2.0–9.0).

At the first examination there was no difference in the proportions of depressive or anxious patients between the operatively (depressed 55%, anxious 62%) and the conservatively treated (depressed 43%, anxious 51%) group (for both $p=0.45$, Fisher's exact test). At the second examination the proportions of both depressive ($p < 0.01$) and anxious ($p = 0.04$) patients differed significantly between the operated and the conservatively treated patients.

Only two (7%) and three (10%) of the operated patients were depressed or anxious, respectively. Four out of five patients who were depressive or anxious preoperatively showed no signs of psychological distress postoperatively. This leaves only three (10%) symptomatic patients in the operative group at follow-up. In contrast, 15 (43%) and 12 (34%) patients were still depressed or anxious, respectively, in the conservatively treated group at follow-up. Eighteen (51%) patients were asymptomatic.

9.7 Factors affecting the outcome of reduction mammoplasty (Study IV)

Patients who were anxious preoperatively had somewhat more improvement in the quality of life index scores when compared to those who were not anxious preoperatively (SF-6D, standardised $\beta = 0.535$, $p = 0.001$; and 15D, $\beta = 0.592$, $p < 0.001$). However, when the mental component summary scores (MCS) of SF-36 were considered, the effect was the opposite: anxious patients having less improvement ($\beta = -0.719$, $p < 0.001$). A similar trend was found with the self-esteem scores of RBDI ($\beta = -0.387$, $p = 0.024$). Preoperatively anxious patients experienced more improvement in the depression score ($\beta = 0.514$, $p = 0.002$). The postoperative “vertical nipple deviation from normal” (ptosis) showed a weak tendency towards less improvement in depression score ($\beta = -0.339$, $p = 0.036$). Patients with physically demanding work experienced somewhat more improvement in SF-6D scores ($\beta = 0.488$, $p = 0.003$) and demonstrated a trend towards less improvement in the mental component summary scores of SF-36 ($\beta = -0.369$, $p = 0.010$). Patients with a single household had a tendency towards less improvement in breast-associated symptoms when compared to patients in a relationship ($\beta = 0.491$, $p = 0.007$). Patients with a body mass index of over 25 tended to experience less improvement in self-esteem ($\beta = 0.390$, $p = 0.023$). For the physical component summary (PCS) of SF-36 or the pain score, no regression models were established as all the tested factors exceeded the limit of statistical significance.

9.8 The medium-term results of reduction mammoplasty (Study V)

The mean follow-up time was 4 years (range 2–5 years). Preoperatively, patients had a significantly inferior quality of life when compared to the age-standardised population (Figure 4). Especially the dimensions of breathing, sleeping, discomfort and symptoms, as well as depression, distress, vitality and sexual activity demonstrated inferior values. This health burden was removed after reduction mammoplasty. Postoperatively, the dimensions for usual activities and mental function showed somewhat better values when compared to the age-standardised population (Figure 5).

At follow-up, patients had fewer breast-associated symptoms, less depression and anxiety and a better quality of life and self-esteem when compared to the preoperative situation (Table 6). The intervention effect of reduction mammoplasty in terms of quality of life (0.083) was more than two and a half times the considered minimal clinically important difference (0.03) of the index score of 15D.

Figure 4. The 15D profiles at baseline (n=62), compared to the age-standardised general female population (n=2468); * significantly worse HRQoL in the patients than the general population at the $p < 0.05$ level, ** at the $p < 0.01$, and *** at the $p < 0.001$ level.

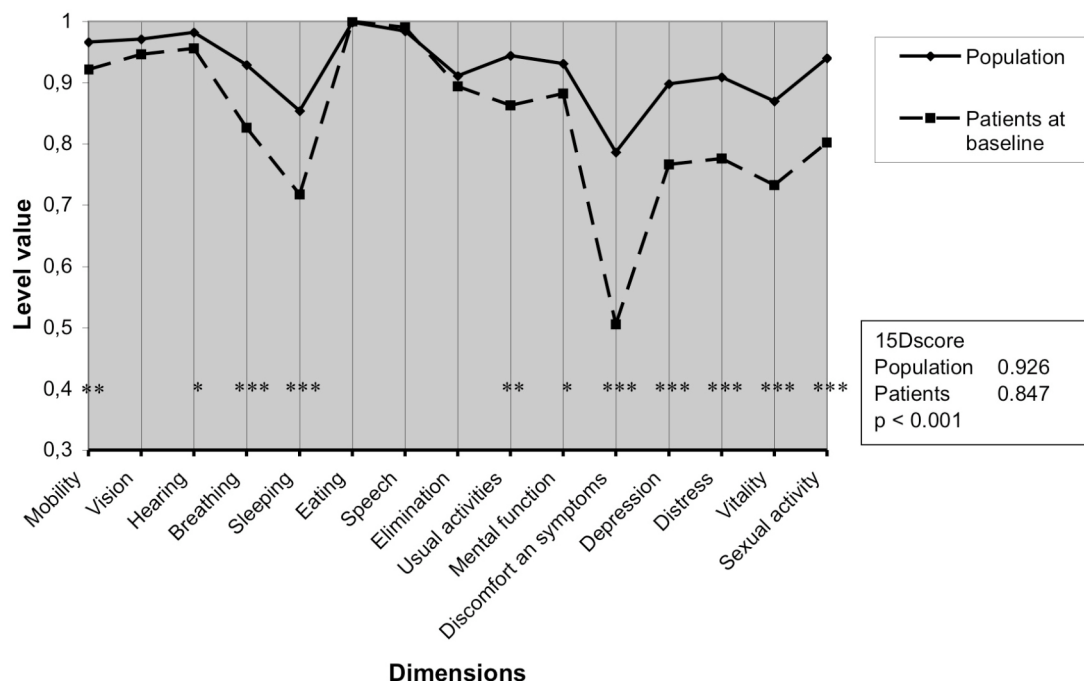


Figure 5. The 15D profiles at 2–5 years follow-up (n=62), compared to the age-standardised general female population (n=2697); * significantly better HRQoL in the patients than in the general population at the $p < 0.05$ level, and ** at the $p < 0.01$.

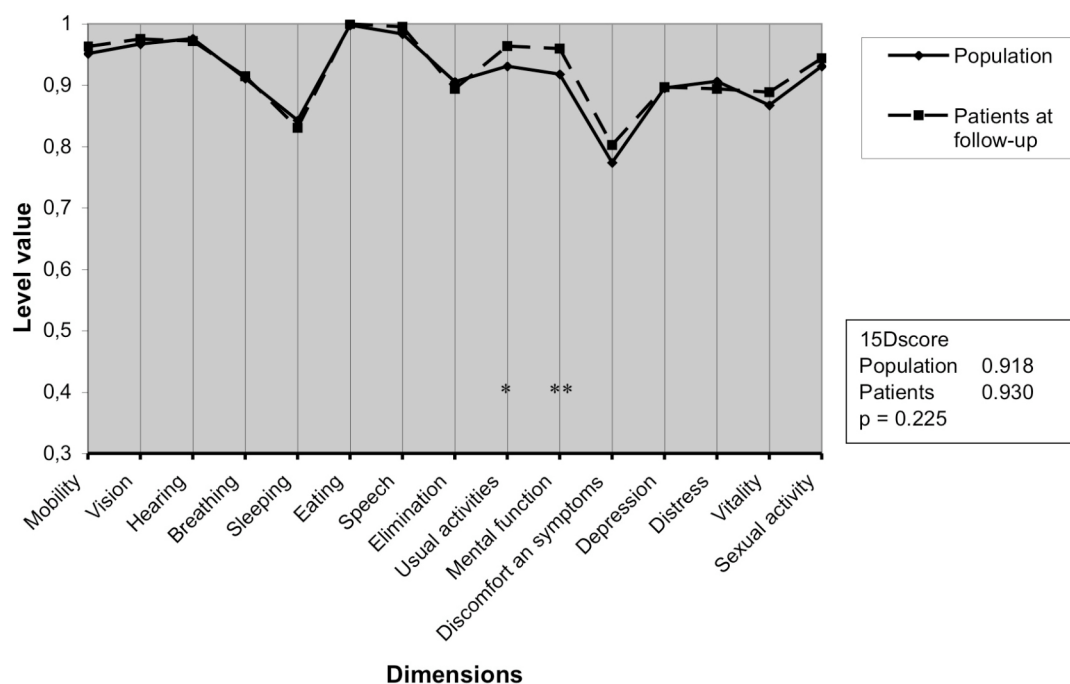


Table 6. Reduction mammoplasty patients' quality of life as well as breast-associated and psychological symptoms at baseline and at 2–5 years' follow-up (n=62).

| | Baseline | Follow-up | <i>p</i> value |
|-----------------------------------|-------------|-------------|----------------|
| 15D score; mean (Sd) | 0.847 | 0.930 | < 0.001 |
| Breast-associated symptoms score; | 59.9 (13.4) | 15.2 (11.0) | < 0.001 |
| Depression score; median | 4 (1-6) | 0 (0-3) | < 0.001 |
| Self-esteem score; median | 4 (2-7) | 6 (4-10) | < 0.001 |
| Anxious; frequency (percentage) | 33 (53) | 8 (13) | < 0.001 |

◇ paired *t* test, † Wilcoxon signed rank test, ‡ McNemar test

10 DISCUSSION

10.1 General considerations

Before the uniform criteria for access to non-emergency treatment in Finland (Finnish Ministry of Social Affairs and Health 2005) came into force on 1 March 2005, the expected waiting time before a reduction mammoplasty operation in the Hospital District of Helsinki and Uusimaa was five to seven years. This may explain why our patients were several years older in comparison to previous prospective study populations (Shakespeare and Cole 1997, Behmand et al. 2000, Blomqvist et al. 2000, Collins et al. 2002, Blomqvist and Brandberg 2004, Freire et al. 2004, Miller et al. 2005, Thoma et al. 2005, Iwuagwu et al. 2006e, O'Blenes et al. 2006, Freire et al. 2007, Neto et al. 2008). In Finland, patients are usually advised to have their children before reduction mammoplasty to ensure successful breastfeeding. Furthermore, cultural differences or the more pronounced low-prioritisation, when compared with countries with insurance coverage systems or criteria concerning maximum times to arrange treatment, may explain the difference. In addition, the criteria for referral and indications for reduction mammoplasty have been strict.

When compared to two recent randomised trials, our patients were also found to be somewhat (Iwuagwu 2003, Iwuagwu et al. 2005, Iwuagwu et al. 2006d, Iwuagwu et al. 2006e) or considerably (Freire et al. 2007, Neto et al. 2008) older. Our patients had a higher body mass index and somewhat greater resection weights. These differences can be explained by reasons discussed above or by exclusion criteria. Freire et al. (2007) and Neto et al. (2008) excluded patients who were over 55 years of age or who had significant co-morbidities, regular medication or a body mass index over 30, as well as those who smoked. In contrast, we included all female patients aged 18–65 years who had bilateral symptomatic breast hypertrophy. Iwuagwu et al. (2006c, 2006d, 2006e) had similar inclusion criteria to ours. They included three and seven current smokers in their intervention (37 patients) and control group (36 patients), respectively. Eighteen patients (22%) in our study population were smokers. Because of these similarities, we find that the results from our randomised trial are comparable to those of Iwuagwu et al. (2006c, 2006d, 2006e), but less so with the results of Freire et al. (2007) and Neto et al. (2008). Some differences are found also in the reduction mammoplasty techniques applied. Iwuagwu et al. (2006c, 2006d, 2006e) used solely the inferior pedicle technique, whereas Freire et al. (2007) and Neto et al. (2008) utilised the superior or superomedial pedicle technique depending on the degree of ptosis. This may explain the differences in resection weights. In our sub-studies a variety of techniques were used depending on the surgeons' and patients' preferences.

The dropout rate (22%) in our randomised trial was quite high and may diminish the significance of our results (Schulz and Grimes 2002). In the other randomised studies the follow-up rate has been higher, varying from 89% to 100% (Iwuagwu et al. 2005, Iwuagwu et al. 2006c, Iwuagwu et al. 2006d, Freire et al. 2007, Neto et al. 2008). Therefore, in comparison to others, our dropout rate yields some weakness

to the otherwise strong scientific evidence produced. However, we found no differences in the baseline characteristics of dropouts and followed patients. This suggests that the dropouts did not bias the results. Our study population size is comparable, and our follow-up time equals or exceeds that of others (Iwuagwu et al. 2005, Iwuagwu et al. 2006c, Iwuagwu et al. 2006d, Freire et al. 2007, Neto et al. 2008). Our study population represented 22 percent of the patients on the waiting list with similar age distributions. We find that our results are well applicable to populations of Finnish breast hypertrophy patients.

10.2 Outcome measurement in reduction mammoplasty

The use of a comprehensive set of standardised and validated tools for assessing the health burden and effects of reduction mammoplasty was introduced by Kerrigan et al. (Kerrigan et al. 2000, Kerrigan et al. 2001). This kind of approach is crucial if adequate and reproducible data for decision-making purposes is to be presented. In addition, the use of quality of life outcome instruments enables a comparison of different health states and treatments (Collins 2003). In this thesis a set of five outcome instruments provided a reliable assessment for the effects of reduction mammoplasty.

However, recently introduced, specifically developed instruments for breast reduction patients provide a better coverage of a larger spectrum of the morbidity of these patients (Sigurdson et al. 2007a, Sigurdson et al. 2007b, Klassen et al. 2009, Pusic et al. 2009). These questionnaires do not suffer from the content validity limitations that the current thesis may be subject to. However, this limitation was compensated in our study by using a set of five questionnaires, as presented in detail in the Methods section. The set of questionnaires used in this thesis covers the same areas as the newly developed instruments. Nevertheless, the questionnaires – with the exception of the breast-associated symptoms questionnaire – have not been specifically developed for reduction mammoplasty patient populations, which brings about some limitations (Pusic et al. 2007a). Firstly, some areas not covered by the new instruments may be included in our questionnaires, making the interpretation of the results different. However, if these areas are assumed not to change after surgery (i.e., not to be related to the health burden of hypertrophic breasts), it can be suggested that any extra areas or remnants included in the questionnaires did not interfere with the results (at most, a weakening effect on the results would have occurred). Changes due to other reasons (for instance, life situations) are possible. Nevertheless, the specifically developed instruments have similar limitations as they also measure somewhat “general” areas (physical, psychosocial and sexual well-being) that may also change due to reasons other than breast reduction surgery. Secondly, the general instruments used in this thesis may have posed responsiveness (sensitivity to change) issues. However, with the exception of the mental summary score of the SF-36 quality of life questionnaire (effect size medium), the effect sizes of our questionnaires were large (over 0.8), suggesting that they responded adequately. Therefore, we find that our set of instruments was able to produce reasonable and adequate results.

10.3 The effects of reduction mammoplasty on quality of life and physical symptoms

The first randomised studies published (Iwuagwu et al. 2006d, Iwuagwu et al. 2006e) provided the long-awaited strong scientific evidence of the effects of reduction mammoplasty. Thereafter, subsequent publications have demonstrated various aspects of the value of reduction mammoplasty (Iwuagwu et al. 2005, Iwuagwu et al. 2006c, Iwuagwu et al. 2006d, Freire et al. 2007, Neto et al. 2008). Iwuagwu et al. (2006d, 2006e) utilised several outcome instruments measuring quality of life and psychosocial factors as an attempt to give a comprehensive and versatile view of the benefits of reduction mammoplasty. Others have concentrated more on functional capacity, pain and self-esteem, and therefore presenting somewhat less diverse results (Freire et al. 2007, Neto et al. 2008). However, none of the previous authors utilised a true condition-specific outcome instrument. All the instruments were otherwise designed for generic use, or originally for other conditions. Therefore we find that our results may provide more adequate data of the benefits of reduction mammoplasty. Although the breast-associated symptoms questionnaire we used has some content limitations (Pusic et al. 2007a, Pusic et al. 2009), it has been noted to yield good internal and external responsiveness (Thoma et al. 2005). However, our questionnaire is a translation of the English version into Finnish. It has not been formally validated, and this is a limitation. A future validation work is therefore required.

Some researchers (Iwuagwu et al. 2006d, Iwuagwu et al. 2006e) have provided their control group with physiotherapy. In our study the non-operative group did not receive any additional treatment. Although physiotherapy has not been found to offer permanent relief (Collins et al. 2002), this could act as an intervention improving the control group thus biasing the results (making the difference between groups smaller). In addition, Iwuagwu et al. (2006d and 2006e) used several outcome measures. They did not, however, take into account the risk of false positive findings due to multiple statistical testing. Nevertheless, their results demonstrated high levels of significance.

Two publications from the same trial found that reduction mammoplasty significantly improved functional capacity and self-esteem, in addition to relieving pain in the lower back, shoulders and neck (Freire et al. 2007, Neto et al. 2008). Freire et al. (2007) and Neto et al. (2008) randomised 100 patients, which is more than in the study of Iwuagwu et al. (2006c, 2006d and 2006e) and the present thesis. However, the patient population was significantly different from those of Iwuagwu et al. (2006c, 2006d and 2006e) and our studies due to exclusion criteria. In addition, Freire et al. (2007) and Neto et al. (2008) also failed to demonstrate the improvement by a condition-specific outcome measure. Nevertheless, their results showed high statistical significance after the six-month follow-up period.

In the current data, reduction mammoplasty resulted in great relief of physical symptoms and pain. This is demonstrated by the physical summary score of the SF-36 and the pain score. Changes in mental health are less obvious or lacking, as demonstrated by the mental summary score of SF-36. These findings are supported by others (Miller et al. 2005, O'Blenes et al. 2006). By alleviating the physical complaints caused by heavy breasts, this surgical treatment provides an excellent improvement in health-related quality of life. However, others have noted that younger women have more psychological symptoms whereas older women

complain more about physical symptoms (Behmand et al. 2000, Sigurdson et al. 2007b). This may explain the above-mentioned findings as the mean age of our patients was 47 years. Freire et al. (2007) and Neto et al. (2008) had considerably younger patients due to their exclusion criteria, but they did not use a psychological outcome measure. Iwuagwu et al. (2006c, 2006d, 2006e) had a patient population that was somewhat younger but otherwise comparable to ours. They used the SF-36 quality of life questionnaire and found significant improvement in both the physical and the mental summary scores. The change in mental health seemed to be greater than in our study. However, they did not present confidence intervals to explore the findings, as we did in our study.

10.4 Comparison to the general population and patients undergoing major joint replacement surgery

The health deficit in patients waiting for reduction mammoplasty is considerable and has been demonstrated in several studies (Klassen et al. 1996a, Klassen et al. 1996b, Shakespeare and Cole 1997, Souza Faria et al. 1999, Behmand et al. 2000, Blomqvist et al. 2000, Kerrigan et al. 2001, Collins et al. 2002, Blomqvist and Brandberg 2004, Freire et al. 2004, Miller et al. 2005, O'Blenes et al. 2006, Thoma et al. 2007, Tykkä et al. 2010). In our study we found that it is comparable to that of patients waiting for major joint arthroplasty (after standardising for age differences). This underlines the fact that symptomatic hypertrophic breasts cause, in our opinion, a true musculoskeletal pain disorder. This is also demonstrated by the condition-specific measure evaluating physical symptoms (Kerrigan et al. 2001, Collins et al. 2002, Miller et al. 2005, Thoma et al. 2007). However, recent research has found symptomatic breast hypertrophy to include components of physical, psychosocial and sexual well-being, and therefore it cannot be considered purely as a condition with physical complaints (Sigurdson et al. 2007a, Sigurdson et al. 2007b, Klassen et al. 2009, Pusic et al. 2009), although the bodily pain and breast-related symptoms are found to dominate (Sigurdson et al. 2007a). The measured health deficit caused by the morbidity (in terms of quality of life measured by a generic instrument) clearly exceeds the minimal clinically important difference and, on the other hand, reduction mammoplasty removes this deficit completely.

Increasing co-morbidity is a common problem in clinical studies, particularly in older patients, and brings limitations to the assessment of the impact of individual conditions on HRQoL (Saarni et al. 2006). Major joint arthrosis usually becomes symptomatic in older patients, whereas hypertrophic breasts are more likely to cause symptoms in early adulthood. A surgical intervention that improves the HRQoL as well as physical, mental and social capability of young people should therefore not be postponed unnecessarily. However, younger women have been noted to have more psychological symptoms, whereas older women complain more about physical symptoms (Behmand et al. 2000, Sigurdson et al. 2007b). Nevertheless, when the pain and disease condition develops within time towards a more chronic condition, coexisting conditions, both physical and mental, can increase and cause further loss of HRQoL (van Elk et al. 2009). The overall approach should be focused on early intervention. This yields more illness-free or

illness-reduced years of life. The burden of coexisting conditions and reduced capacity to heal with increasing age, as shown in total joint replacement (Rissanen et al. 1997), can hinder rehabilitation and produce less satisfactory results.

When compared to patients waiting for major joint arthroplasty, the quality of life of patients awaiting reduction mammoplasty was somewhat better preoperatively, when results were standardised for age. This is probably because fewer co-morbidities were present. This may explain why patients who have undergone reduction mammoplasty may experience an even greater improvement in HRQoL than those who have received major joint replacement, because significant co-morbidities do not prohibit receiving full benefit from the procedure. This further underlines the importance of early intervention. Furthermore, all secondary consequences of symptomatic hypertrophic breasts (sick leaves for musculoskeletal symptoms, costs of pain medication and physiotherapy, etc.) are reduced or removed. In the end, the gain of an individual patient is much more than what can be calculated by means of cost-effectiveness analysis. However, defining cost-effectiveness offers a crucial tool for financial decision-making.

10.5 The effects of reduction mammoplasty on psychosocial symptoms

Studies on psychological changes after breast reduction have used various instruments, most commonly the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith 1983). In our study we used Raitasalo's modification of the short form of the Beck Depression Inventory questionnaire (Raitasalo 2007). However, recently developed condition-specific instruments include psychosocial aspects perhaps obviating complementary psychological questionnaires (Sigurdson et al. 2007a, Sigurdson et al. 2007b, Klassen et al. 2009, Pusic et al. 2009). Nevertheless, psychological evaluation may be recommended preoperatively as some of the patients may need psychological intervention before surgery (Rubino et al. 2007, Kellett et al. 2008). On the other hand, additional preoperative information has also been found to reduce anxiety (Danino et al. 2005).

Preoperatively we found half of the patients to be depressed or anxious, or both. This high psychological morbidity has also been shown by others (Guthrie et al. 1998, Souza Faria et al. 1999, Iwuagwu et al. 2006d, Benditte-Klepetko et al. 2007). It has been suggested that patients whose macromastia becomes symptomatic and who ask for reduction mammoplasty are vulnerable to adverse comments about the size of their breasts (Guthrie et al. 1998), and their interpersonal sensitivity and hostility is greater (Behmand et al. 2000). The increasing weight of breasts may correlate with more depressive symptoms (Benditte-Klepetko et al. 2007). However, there is also a correlation between obesity and depression (Herva et al. 2006), and so weight loss may reduce psychological risks (Benditte-Klepetko et al. 2007). Obesity is also associated with poorer self-esteem (Sarwer et al. 2005). In our patient population, four out of five subjects showed no signs of their preoperative depression or anxiety six months after reduction mammoplasty. In the conservatively treated group the incidence of depression remained unchanged during the follow-up period. However, the patients were slightly less anxious at the second examination. This may be explained by the

fact that they already knew their operation would come within the following months and felt relieved.

Two earlier studies have reported an improvement in psychological well-being in patients who requested reduction mammoplasty for cosmetic reasons (Hollyman et al. 1986, Chahraoui et al. 2006). The results are therefore not directly comparable with those in our study. Nevertheless, four prospective studies (Souza Faria et al. 1999, Behmand et al. 2000, Borkehagen et al. 2007, Mello et al. 2009) and three randomised trials (Iwuagwu et al. 2006d, Iwuagwu et al. 2006e, Neto et al. 2008) have reported on psychological symptoms among patients with symptomatic hypertrophic breasts. However, in one of the prospective studies (Souza Faria et al. 1999), the follow-up time was quite short for some patients, ranging from one month to 10 months (mean 4), and the clinical details were not available for comparison. Of the other three prospective studies, results ranged from good to somewhat weaker evidence (Behmand et al. 2000, Borkehagen et al. 2007, Mello et al. 2009). Two randomised trials (Iwuagwu et al. 2006d, Iwuagwu et al. 2006e) reported results with the same group of patients. The first report focused on quality of life and also introduced psychosocial changes. The other assessed changes in depression and anxiety. In both, breast reduction had a significantly good impact on quality of life, depression, anxiety, and psychosocial aspects. In comparison with our study, the follow-up time (four months) was somewhat shorter and the patients were younger, but the size of breasts, height, and weight of the patients were roughly similar. The third randomised study also showed the improvement in patients' self-esteem after reduction mammoplasty (Neto et al. 2008).

In comparison to our study, more residual anxiety postoperatively was reported by Souza Faria et al. (1999). In our study, the excess of depression and anxiety were reduced in equal amounts, but there was still some residual depression and anxiety left. Nevertheless, the amount was small, and comparable to "normal" levels in the general population (Kurki et al. 2000).

Younger women have been noted to have more psychological symptoms whereas older women complain more about the physical symptoms (Behmand et al. 2000, Sigurdson et al. 2007b). Although our patients were older (mean age 47 years, range 22–64), they presented significant psychological symptoms preoperatively. This may reflect that chronic pain may cause psychosocial morbidity over the years (van Elk et al. 2009). This factor may have been important in our patient population, as the waiting time for the operation was five to seven years.

10.6 Factors affecting the outcome of reduction mammoplasty

Past studies have suggested dissatisfaction with the outcome to be related to anxiety and depression (Cerovac et al. 2005, Chahraoui et al. 2006). Recent qualitative research has shown that psychosocial aspects are fundamental in the measurement of the outcome of reduction mammoplasty (Sigurdson et al. 2007a, Sigurdson et al. 2007b, Klassen et al. 2009, Pusic et al. 2009). In fact, less psychological distress preoperatively seems to improve outcome (von Soest et al. 2006). An increasing number of co-morbid conditions have been found to have a

deteriorating effects on outcome (Collins et al. 2002). Some authors have suggested a higher body mass index to be associated with poorer clinical outcome (O'Grady et al. 2005, Villani et al. 2009), while others have not found obesity to increase complication rates (Setälä et al. 2007, Roehl et al. 2008). The quality of the preoperative information provided and the relationship between the patient and surgeon are also associated with patient satisfaction or dissatisfaction (Chahraoui et al. 2006). Unfortunately, preoperative information seems to be retained poorly by patients (Godwin 2000), but a written consent provides better understanding (Ashraff et al. 2006). Audiovisual material has been found to reduce anxiety and improve knowledge (Danino et al. 2005).

In Study IV, we found some interesting associations between psychosocial factors and the outcome measure changes. Although the true effects of reduction mammoplasty are a result of the weight reduction of the breasts, some differences in the outcome are explained by patient-related factors. Anxious patients or those with physically demanding work improved less. The expectations of these patients may have been unrealistic as breast reduction is not the treatment of choice for psychological disorders or decreased work capacity, although it certainly reduces the overall physical and psychological distress. A discrepancy between patient expectations and the attainable benefit may have caused disappointment and a decrease in mental health (Montebarocci et al. 2007, Rubino et al. 2007).

Patients with no overweight had a trend towards better improvement in self-esteem when compared with those whose body mass index was over 25. This may be explained by a negative effect of overweight on self-esteem (Sarwer et al. 2005) and body-image (von Soest et al. 2009). However, patients with a greater body mass index or greater resection weight seem to gain more improvement after breast reduction in terms of breathing function (Sood et al. 2003, Iwuagwu et al. 2006c). The patients in our study weighed 0.5 kg more after the breast reduction, when an adjustment for the breast resection weight was made. Some authors have suggested a stimulus for weight loss after breast reduction (Singh et al. , O'Blenes et al. 2006). Our follow-up time was somewhat shorter, which may explain why patients were not able to reach the full benefit from the procedure. On the other hand, patients have been strongly advised to lose weight before surgery to minimise complication risks and the small weight gain afterwards may be only a return to "normality." However we had no objective information of the weight status before the first examination, and this question therefore remains unanswered to a degree.

10.7 Medium-term results of reduction mammoplasty

The short-term result may change over time, which is why medium and long-term evaluation is essential to verify the results. In this thesis medium-term results were collected after a mean of four years' (range two to five years) follow-up. At this point possible factors affecting short-term results, as complications or euphoria, have subsided. Prospective long-term (i.e., 10 years or more) follow-up data on reduction mammoplasty is lacking. The outcome of reduction mammoplasty seems to remain stable at two to four years' follow-up (Shakespeare and Postle 1999, Blomqvist and Brandberg 2004, O'Blenes et al. 2006). However, questions arise as some impairment has been noted during follow-up. Blomqvist and Brandberg

(2004) reported a small non-significant increase in patient-reported pain, especially headache, from one to three years follow-up. They concluded these changes to be connected to other factors than breast problems. However, a similar trend was also noted in patient-reported problems related to breast size and weight.

In our study, a subgroup analysis of our previous data at six months' follow-up (Studies I and III) demonstrates that the effects of breast reduction surgery remain stable with no significant loss during the first postoperative years. In fact, our medium-term follow-up data shows slightly better results when compared with the six-month data. This differs from previous studies reporting a so-called "honeymoon effect" with some loss of the positive outcome at medium-term follow-up (Blomqvist and Brandberg 2004, O'Blenes et al. 2006). Our patient population also showed significantly better values in some dimensions (usual activities and mental health) when compared to the age-standardised general population at two to five years' follow-up. This is in contrast to previous studies (Blomqvist and Brandberg 2004, O'Blenes et al. 2006). Although our prospective follow-up study did not have a true control group, the above findings strongly suggest that the surgical result remains stable from short to medium-term (two to five years) follow-up.

10.8 Future prospects

The introduction of new outcome instruments hopefully provides better and adequate tools for assessing the condition caused by symptomatic hypertrophic breasts (Sigurdson et al. 2007a, Sigurdson et al. 2007b, Klassen et al. 2009, Pusic et al. 2009). Nevertheless, one of these questionnaires needs to be translated into Finnish, and this requires resources and sample sizes that can only be achieved by cooperation between several centres. However, in the present circumstances, when resources are continuously restricted, general outcome measures should complement these condition-specific instruments to allow us to compare the effects of different surgical treatments and medical conditions (Pusic et al. 2008, Cano et al. 2009, Pusic et al. 2010). Overall, a standardised, multi-centre data collection protocol would best serve both patients and plastic surgeons. This would provide data needed for updating the uniform criteria for access to non-emergency treatment of symptomatic breast hypertrophy. It will be challenging, maybe impossible, to set rigorous threshold levels for the medical necessity of reduction mammoplasty. However, adequate data collection will certainly provide valuable assistance for the clinical decisions.

Although randomised controlled trials (RCTs) provide the most scientifically precise evidence, new RCTs with longer follow-up periods (up to one year, or even more) are probably not possible due to practical and ethical reasons. Instead, RCTs with larger patient populations could be valuable, especially with new outcome measures, as discussed above. Meanwhile, long-term (i.e., 10 years or more) follow-up studies are required to further substantiate the value of reduction mammoplasty. Also with these, a standardised data collection protocol is indispensable to achieve adequate and solid evidence.

11 CONCLUSIONS

1. Reduction mammoplasty significantly improves quality of life and alleviates breast-associated symptoms and pain. Changes in the physical health were highly significant, whereas changes in the mental health were somewhat less pronounced.
2. Reduction mammoplasty significantly alleviates depression and anxiety, and restores patients' self-esteem. Preoperatively, half of the patients were depressed or anxious, or both. After reduction mammoplasty, four out of five showed no signs of depression or anxiety.
3. Symptomatic breast hypertrophy causes an appreciable loss of health-related quality of life when compared to the age-standardised general population. This health deficit is removed by reduction mammoplasty.
4. The extent of the health deficit of symptomatic breast hypertrophy is similar to that caused by symptomatic major joint arthrosis. Preoperatively reduction mammoplasty patients had somewhat better quality of life than major joint replacement populations when results were standardised for age.
5. The effects of reduction mammoplasty in terms of health-related quality of life are comparable to those of major joint replacement. The intervention effect is the same as in total hip joint replacement and more than two times that of total knee joint replacement. The intervention effect of reduction mammoplasty (in terms of quality of life) is two times the minimal clinical important difference.
6. The outcome of reduction mammoplasty is affected more by preoperative psychosocial factors than by changes in breast dimensions. Especially preoperative anxiety was associated with outcome differences in the patient population.
7. The effects of reduction mammoplasty remain clearly significant and stable at two to five years' follow-up. This is demonstrated by fewer breast-associated symptoms and decreased psychological morbidity, as well as a better quality of life. A "honeymoon effect" was not detected, as the medium-term results were somewhat better than the short-term (6 months) results.

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