The Effects of Breast Reduction on Back Pain and Spine Measurements – A Systematic Review

&

Breast Hypertrophy – A Real Pain in The Back

Constantine Papanastasiou, MD

MSc Candidate – Experimental Surgery

Division of Plastic and Reconstructive Surgery

Department of Surgery

McGill University, Montreal

Submitted: August 2019

A manuscript-based thesis submitted to McGill University in partial fulfillment of the requirements of the degree of Master of Science.

TABLE OF CONTENTS

ACKNOWLEDGEMENTS

We would like to express our gratitude to the MRI team at the Montreal General Hospital and the EOS team at the Shriners and Glen MUHC. We would also like to thank the Plastic Surgery Foundation (PSF) for the research grant awarded to this study. Thank you to Dr. Maryse Fortin for the MRI analysis. Thank you to Dr. JR Garcia Luna for the data analysis. Thank you to my co-supervisor Dr. Ouellet whose expertise and guidance helped shape this paper for the orthopedic spine component.

Finally, thank you to my supervisor Dr. Lessard. Several years ago, Dr. Lessard came up with the idea for this prospective study between cases at the Montreal General Hospital. As a dedicated surgeon and passionate researcher, she put together a highly specialized team to see this project through to its completion. Thanks to her innovation and ability to think outside the box, this study has been a true success. Coaching me thoroughly for my two podium presentations at the Plastic Surgery Research Council, Dr. Lessard has been an ever-present source of guidance, knowledge, and experience. I will forever be grateful for the opportunity.

Chapter 1: The Effects of Bilateral Breast Reduction on Back Pain and Spine Measurements – A Systematic Review

Abstract (Eng)

Background

The aim of this review article was to synthesize the literature on reduction mammaplasty and its effects on the spine. The particular focus was to find these few radiological studies and those investigating changes in spinal angles, posture, center of gravity, and back pain reduction.

Methodology

We performed a thorough review of the literature, searching the Medline database for all relevant published data studying reduction mammaplasty and the spine. The search yielded 107 articles of which 11 articles met our specific inclusion criteria. The primary outcome measures of the studies as well as their respective results were tabulated, contrasted, and compared.

Results

The 11 cohort studies included in this review cover the period from 2005 to 2015 and focus on breast hypertrophy and spine. According to these 11

quantitative studies, breast hypertrophy causes objective, quantitative, measurable disturbances to women living with this condition. Reduction mammaplasty produces an unmistakable improvement in signs, symptoms, and quantifiable measures. Although the majority of included papers in this review described postoperative improvement in spinal angles, there remain discrepancies of results between them.

Conclusions

The studies included in this review did offer a promising glimpse into the complex interaction between breast hypertrophy and the spine. However, future research initiatives can improve upon what these investigators have begun with more refined, objective, radiological evidence. More specifically, we aim to clarify some of the basic hypotheses in our center with the use of EOS®.

ABSTRACT (FR)

Contexte

Le but de cet exposé de synthèse fut de condenser la littérature sur la réduction mammaire et ses effets sur la colonne vertébrale. Une attention particulière a été mise sur les rares études radiologiques et celles investiguant les changements au niveau des angles spinaux, de la posture, du centre de gravité et de la douleur.

Méthodologie

Nous avons effectué un examen approfondi de la littérature, passant au peigne fin la base de données Medline, à la recherche de toute étude publiée pertinente sur les réductions mammaires et la colonne vertébrale. Parmi les cent sept articles de haute qualité qui se sont démarqués, onze articles ont rencontré nos critères d'inclusion spécifiques. Le principal indicateur des résultats ainsi que leurs données respectives furent tabulés, mis en évidence et comparés.

Résultats

Les 11 études de cohorte d'observation prospectives incluses dans cette revue couvrent la période de 2005 à 2015 et se concentrent sur l'hypertrophie mammaire et la colonne vertébrale. Selon ces 11 études quantitatives,

l'hypertrophie mammaire cause des perturbations objectives, quantitatives et mesurables chez les femmes atteintes de cette condition. La réduction mammaire produit une amélioration indubitable des signes, des symptômes, et des mesures quantifiables. Bien que la majorité des articles inclus dans cette revue décrit l'amélioration postopératoire des angles de la colonne vertébrale, il y a divergence au niveau des résultats.

Conclusion

Les études incluses dans cette revue ont offert un aperçu prometteur de l'interaction complexe entre l'hypertrophie du sein et la colonne vertébrale. Toutefois, de futures initiatives de recherche peuvent améliorer ce que ces chercheurs ont amorcé grâce à des preuves radiologiques plus détaillées et objectives. Plus précisément, nous visons à clarifier certaines des hypothèses de base avec l'utilisation de EOS®.

Contribution of Authors

Constantine Papanastasiou, MD, MSc(c) - first author, data acquisition & analysis

Jean A. Ouellet, MD, FRCSC – co-author, orthopedic collaboration

Lucie Lessard MD, FRCSC, FRCSC, FACS – corresponding and senior author, principal investigator

BACKGROUND

Breast hypertrophy is responsible for a broad array of patients' signs and symptoms ranging from mild to debilitating in nature. The most common physical complaints include neck and upper back pain, headache, aching shoulders, painful shoulder grooves, low back pain, intertrigo of the inframammary crease, mastalgia, poor posture, difficulty exercising, and difficulty working a job without absenteeism.[1-3] General back pain is known to be the most expensive disease regarding work absenteeism/disability representing up to 1.75% of the gross national product (GNP) of some countries and 20.6% of National Health Insurance Survey (NHIS) respondents reporting lower back pain.[4] [5] Breast hypertrophy patients are no exception to these statistics. The mass of hypertrophied breast glands imposes downward traction on the musculofascial sling surrounding the shoulders and neck, namely the trapezius, levator scapula, and rhomboid.[6, 7] There is also increased pressure on the greater occipital nerve, lesser occipital nerve, and dorsal occipital nerves. This was confirmed by Mosser et al. in a cadaver study of 20 heads from patients with an unknown history of migraine headaches.[8]

The most effective treatment for breast hypertrophy and its accompanying signs and symptoms is bilateral breast reduction surgery: vertical or horizontal techniques. According to satisfaction survey questionnaires and meta-analysis studies, it has been repeatedly proven to be a surgical procedure with a very high patient satisfaction rate.[9, 10] In a study by Brown et al. a satisfaction rate of 89%

was demonstrated.[9] It is hypothesized that the center of gravity reverts to its more neutral position posteroinferiorly. The spine returns to a more neutral curvature, allowing the paraspinal muscles to relax. As such, pain is alleviated.[11] Until relatively recently, the scientific documentation was not totally adequate with the exception of validated satisfaction questionnaires such as the Breast-Q satisfaction outcomes. [12-15] In addition to the physical disturbances, macromastia has a significant negative impact socially, personally, and as it relates to self-esteem and health-related quality of life of patients.[16]

The aim of this review article was to synthesize the literature on reduction mammaplasty and its effects on the spine before and after surgery. The particular focus was to find all radiological studies and those investigating changes in spinal angles, posture, center of gravity, and the relation to pain reduction.

The spine attempts to stay in balance using the least amount of energy possible and preferably in a neutral position. The excessive weight of hypertrophic breasts acts as a lever to disrupt stabilizing forces of the neck and back. The center of gravity of the body is altered moving superiorly and anteriorly during daily activities. This results in an altered curvature of the spine resulting in increased lumbar lordosis, thoracic kyphosis, and cervical lordosis. There is an ensuing compensatory contraction of the paraspinal muscles. This constant muscle contraction can cause significant and persistent pain requiring chronic pain control medication around the clock in many patients just to get through the day. [11, 17]

METHODOLOGY

Inclusion criteria were English and French language publications, human subjects, bilateral reduction mammaplasty, extractable outcomes, and full-text availability. Our aim was to find the studies in the literature studying the effects of breast hypertrophy on the spine. PubMed was used to search all relevant published data studying reduction mammaplasty and the spine from the Medline database of the U.S National Library of Medicine. The searches were conducted in July 2017. Using PubMed, the search strategy combined combinations of keywords “breast reduction”, “reduction mammaplasty”, “spine”, “spinal”, “vertebral”, “posture”, “back”, and “skeletal”. The resultant articles were assessed, and their references were inspected for further articles pertinent to this review. The search yielded a total of 107 citations. Ninety-seven of the papers did not match our inclusion criteria because they did not combine analyses of both breast and spine interaction. One article found in the references of an included paper was subsequently added as it met our inclusion criteria. The remaining 11 articles met our inclusion criteria and were suitable for analysis (See Figure 1). The selected studies were graded using the University of Oxford Center for Evidence Based Medicine Levels of Evidence (See Figure 2). The data from the selected articles are presented in Table 1. The primary outcome measures of the articles as well as their respective results are displayed. Initially, a meta-analysis of the studies was contemplated. However, this was deemed unfeasible as the outcome measures and methodology differed too drastically even between those few studies, suggesting the need to study this subject in better depth.

RESULTS

The articles included in this in-depth review cover the period from 2005 to 2015 and focus on breast hypertrophy, back pain, and spine. The 11 studies included in this review had sample sizes ranging from n=10 to n=50. Table 1 summarizes the data with regards to type of study, cohort size, outcome measures, and results.

REVIEWED STUDIES CHARACTERISTICS

A total of 11 studies were included in this review from 2005 to present. The two studies by Benditte et al. and Krapohl et al. examined women with breast hypertrophy, in the non-surgical setting. Nine studies evaluated a cohort of breast hypertrophy patients both preoperatively and postoperatively.[18-26] The studies by Sahin et al., Lapid et al., Barbosa et al., Tenna et al., Foreman et al., and Krapohl et al. were non-radiological and more external measurement based. These six studies used 3D gait analysis, back inclination angle, center-of-pressure displacement, center-of-gravity oscillations, lower back compressive force, and functional spine score respectively.[1, 20, 21, 24-26] Five of the studies were radiological in nature.[18, 19, 22, 23, 27] The studies by Berberoglu et al., Karabekmez et al., Karaaslan et al., and Findikcioglu et al. used regular X-rays to compare preoperative and postoperative spinal parameters while Benditte et al. used magnetic resonance imaging (MRI). Some of the outcome measures of these radiological studies included cervical lordosis angle, thoracic kyphosis angle, lumbar lordosis angle, lumbosacral inclination, and sagittal balance disturbance.[18, 19, 22, 23] In addition to MRI, Benditte et al. made use of the Visual Analog Scale (VAS) pain score and the Beck Depression Inventory (BDI).[27]

Spinal Angles – Cervical, thoracic, and lumbar

Only five previous studies compared reduction mammaplasty patients' preoperative and postoperative spinal angles.[18, 19, 21-23] Three studies found positive improvement. Berberoglu et al. found a statistically significant decrease in cervical lordosis (CL) (9.9±0.9, p<0.001) and thoracic kyphosis (TK) (17.0±6.1, p<0.001).[18] Karabekmez et al. also demonstrated significantly improved CL (8.7±3.7, p<0.001), TK (13.9±4.3, p<0.001), and improved sagittal balance (p = 0.008).[19] Improvement in TK (-2.7, p<0.001), lumbar lordosis (LL) (-3.2, p<0.001), and sacral inclination angle (-0.9, p=0.005) were found by Findikcioglu et al.[23]

Two studies were not statistically significant. Those two studies are the following:

Lapid et al. with no statistically significant improvement in back inclination angle (0.89±3.48 t=0.104) and Karaaslan et al. with no statistically significant improvement in TK and LL.[21, 22]

Gait, Center of gravity, and Sagittal balance

Karabekmez et al. demonstrated a postoperative return to normal sagittal balance in all seven patients with disturbed sagittal balance preoperatively.[19] Sahin et al. used 3D gait analysis on ten patients to demonstrate a statistically significant improvement in maximum anterior pelvic tilt (41% reduction), average maximum spine anterior flexion (30% improvement), and an improved body posture when walking after breast reduction surgery.[20] In the study by Barbosa et al. it was demonstrated that postoperative patients had a smaller center-of-displacement area and improved postural control.[24] Tenna et al. demonstrated, by means of static stabilometry, that postoperative reduction mammaplasty patients have objectively improved posture at the 6 month postoperative mark (p=0.032).[25]

Spine MRI, spine score, functional spine score, & lower back compressive force

Benditte et al. 2007, utilized MRI to investigate fifty breast hypertrophy patients for degenerative changes in the thoracic and cervical spine more specifically. The investigators evaluated “loss of signal characteristics, posterior and anterior disc protrusion, narrowing of the disc space, and foraminal stenosis” as well as deviations in the frontal and sagittal plane.[27] Their results demonstrated breast weight had a statistically significant positive effect p=0.02 on pathological findings such as spine score (0.71, p<0.0001), pain (0.69, p<0.0001), BDI (0.58, p<0.0001), and (BMI) (0.57, p<0.0001). Age also had a statistically significant positive improvement correlation with pathological findings (p = 0.03).[27] These papers confirm that breast hypertrophy overloads the spine leading to advanced degenerative disease. In another prospective study but with a small cohort of patients, Foreman et al. found that postoperatively, their eleven reduction mammaplasty patients had a 35% decrease in low-back compressive forces.[26] Such findings of change in center of gravity post breast reduction is in keeping with the offloading of the musculature.

Pain and Relief

Lapid et al. reported that preoperatively, 71.4% of their subjects had a higher VAS pain score. This statistic improved postoperatively with 19.0% patients reporting a higher VAS pain score.[21] Barbosa et al. revealed an improvement in shoulder and neck pain, headache, hand numbness and upper/lower back pain.[24] The investigators attributed this symptom relief to an improvement in postural control. [24] Participants in the study by Foreman et al. demonstrated a 76% postoperative reduction in self-reported disability, with the greatest improvements in the categories for frequency of pain and discomfort with travel.[26] Benditte et al. found a significant correlation r between pain and breast weight (0.69, p<0.0001), MRI score (0.46, p=0.0012), spine score (0.75), BDI (0.61, p<0.0001), and BMI (0.58, p<0.001)".[27]

Body Mass Index and Posture

In the study by Berberoglu et al., there was no significant correlation found between postoperative vertebral angle and patient BMI. However, Karabekmez et al. established significant correlations between BMI and total excised breast tissue volume (p=0.0001) and ΔCL angle postoperatively (p=0.03).[19] Lapid et al. found that back inclination was dependent on the BMI of the patient (-0.274, p=0.001). In the study by Findikcioglu et al., it was determined that BMI had a significant correlation with preoperative thoracic kyphosis (r=0.700, p<0.001), lumbar lordosis (r=0.740, p<0.001), and sacral inclination angle (r=-0.005, p=0.977).[23] The study conducted by Benditte et al. demonstrated that BMI could prompt the development of spine disorders, postural anomalies, and depressive symptoms. In addition, they found a statistically significant correlation r between BMI and breast weight (0.57, p<0.0001), spine score (0.51, p=0.0001), and pain (0.37, p<0.0001).[27] In a study of n=346 patients by Coltman et al. it was also demonstrated that BMI had a significant main effect on breast volume. In fact, the median breast volume of obese subjects was nearly triple that of their counterparts with normal BMI.[28]

DISCUSSION

We are presently studying back pain in breast hypertrophy patients with EOS at our University center and this is why we have embarked on this in-depth scientific review of this topic.[29] Even presently in 2018, quantitative tests to evaluate patients' back pain before and after surgery are still less than optimal.[30, 31]

On this topic in the literature, 107 scientific papers were found, but only 11 were valuable scientific papers with quantitative measures. Breast hypertrophy causes objective, quantitative, measurable disturbances in women living with this condition.[30] It results in pain and fatigue that can negatively affect these women severely in their day-to-day life at home and especially at work. This makes their work productivity levels difficult to maintain. In a study by Cabral et al. it was scientifically demonstrated that breast reduction results in a significant decrease in working hours lost, impairment at work, overall productivity loss, as well as daily activity impairment outside of work.[32] Validated questionnaires were used to report those symptoms in a quantitative fashion. In general, back pain is on the rise as a major health burden especially with increasing rates of morbid obesity and rising BMI.[33] In a study conducted in the Netherlands, the cost of back pain was found to be substantial enough to represent 1.7% of the country's gross national product and the most expensive disease regarding work absenteeism and disability. [5]

The well-validated Breast-Q study standard questionnaire for evidence-based breast surgery revealed that over 95% of patients were pleased post breast reduction and 96% of those would "do it again"[34]

On the other hand, pure quantitative self-esteem assessment was reported using the Multidimensional Body Self-Relations Questionnaire (MBSRQ) and clearly demonstrated breast hypertrophy's negative effects on self-esteem. [31]

Another valuable quantitative tool is the classic Visual Analog Scale (VAS). Breast hypertrophy patients did score highly, with 10 being the worst pain on this scale. One study demonstrated a VAS score reduction from 69.5 preop to 13.3 postop.[18] Breast hypertrophy causes immense pain for patients as mentioned above on the VAS scale. In all studies that applied a component of pain evaluation, a significant improvement in pain postoperatively was demonstrated.[18, 21, 24, 26, 27]

The mechanism by which this pain reduction is achieved is still not fully understood. It is likely a multifactor sequence of transformations in the spine, its ligamentous attachments, and possibly tension in the paraspinal musculature as well. In addition, this pain alleviating mechanism in itself deserves further study.[29]

It has been presumed that a change in spinal angles may occur postoperatively after reduction mammaplasty, but only few studies have explored this clinical question. Five studies in this review compared preoperative and postoperative spinal angles. Statistically significant improvement was demonstrated in three of the five studies.[18, 19, 23] On the other hand, the two other studies did not demonstrate any significant angle correction.[21, 22] Even in the few studies looking at the spinal angles in a quantitative manner, there is contradiction. In those five studies, cervical lordosis and thoracic kyphosis angles appear to correct to a higher and more consistent degree than does lumbar lordosis angle. Although the majority of included papers in this review described postoperative improvement in spinal angles, there remain discrepancies of results between them.

In addition, the radiological studies did reveal their respective weaknesses. The study by Berberoglu et al. used reference values for incline angles from the general population. It would have been more interesting to find these values for their study population as well as the variation between age and sex groups.[18] Findikcioglu et al. stated their greatest limitation to be the fact that vertebral angles vary widely in the population and as such the reference range is equally wide.[23] Finally, the study by Benditte et al. excluded obese women and women over 40 years of age. This may have caused their cohort to be unrepresentative of the typical population seeking breast reduction since they have a high BMI and they are over 40 years of age in most cases.

In summary, the eleven studies extracted and available in the literature fitting all the inclusion criteria from 107 studies, are the only ones which have made attempts at quantifying back pain in breast hypertrophy. We have reviewed these papers to evaluate the different technologies (PT, X-Ray, and MRI) presently available to quantify pain and discomfort of breast hypertrophy. The results are summarized and presented in Table 1 and Table 2.

Despite their limitations, the 11 papers selected for this study provide an initial contribution. With this thorough review, the 5 best imaging-based scientific papers revealed conflicting results such as positive improvement versus no improvement for the same breast pathology. The literature is contradictory at best for a surgery with a 95% Breast-Q postoperative satisfaction and 96% of those patients who would "do it again" given the option.[34]

In conclusion, this systematic review confirms that there is room for further future studies with better quantitative tools and methodology.

Tables and Figures

TABLE 1: COHORT STUDIES: COHORT, OUTCOME MEASURES AND RESULTS

Study	Cohort	Outcome measures	Results
Berberoglu et al. 2015	40	CL (Cervical Lordosis), TK (Thoracic Kyphosis), LL (Lumbar Lordosis), LSI (Lumbosacral Inclination), back pain alleviation	Improvement in all spinal angles, decreased back pain
Karabekmez et al. 2014	22	CL, TK, LL, SBD	Improvement in all spinal angles, SBD corrected
Sahin et al. 2013	10	3D gait analysis (APT, SAF angles)	Improvement in APT, SAF, and in body posture when walking
Lapid et al. 2013	42	Back inclination angle	No statistically significant improvement in back inclination angle
Karaaslan et al. 2013	34	TK, LL	No statistically significant improvement in TK or LL
Findikcioglu et al.	30	TK, LL, LSI	Improvement in all spinal angles

2013			
Barbosa et al. 2013	14	Center-of-pressure displacement	Significant improvement in postural control
Tenna et al. 2012	30	Center-of-gravity oscillations	Improvement in posture
Foreman et al. 2009	11	Lower back compressive force	35% reduction in lower back compressive force
Benditte et al. 2007	50	MRI, spine score, VAS pain score, BDI	Increasing breast weight correlated with degenerative spine disorders and depressive symptoms
Krapohl et al. 2005	50	Functional spine score	Spinal function significantly impaired with increasing breast weight

TABLE 1 NOTE: ABBREVIATIONS: CL (CERVICAL LORDOSIS), TK (THORACIC KYPHOSIS), LL (LUMBAR LORDOSIS), LSI (LUMBOSACRAL INCLINATION), SBD (SAGITTAL BALANCE DISTURBANCE), APT (ANTERIOR PELVIC TILT), SAF (SPINE ANTERIOR FLEXION), BDI (BECK DEPRESSION INVENTORY)

TABLE 2: HIGHLIGHTED SPINAL ANGLE FINDINGS

Study	Cohort	∆CL	∆TK	∆LL	∆ Back Inclination Angle	Sagittal Balance
Berberoglu et al. 2015	40	-9.9±0.9 p<0.001	-17.0±6.1 p<0.001			
Karabekmez et al. 2014	22	-8.7±3.7 p<0.001	-13.9±4.3 p<0.001			Improvement p=0.008
Lapid et al. 2013	42				No significant improvement	
Karaaslan et al. 2013	34		No significant improvement	No significant improvement		
Findikcioglu et al. 2013	30		-2.7, p<0.001	-3.2, p<0.001		

FIGURE 1: ARTICLE SELECTION FLOW CHART

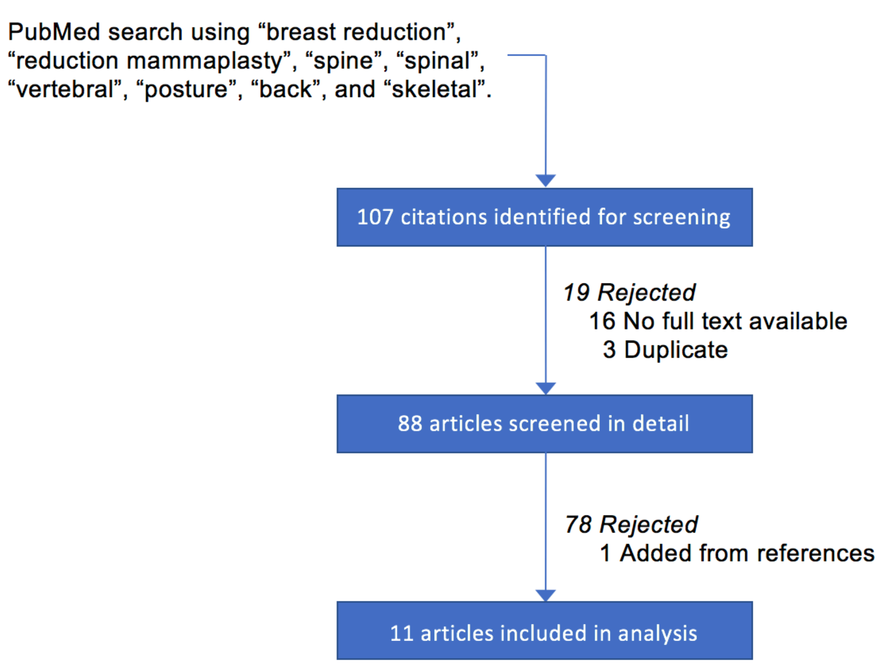


FIGURE 2: UNIVERSITY OF OXFORD CENTER FOR EVIDENCE BASED MEDICINE - LEVELS OF EVIDENCE

Level	Description
1A	Systematic review of randomized control trials with homogeneity
1B	Individual RCT
1C	All or none (e.g. all had a particular outcome prior to an intervention and now no such outcomes occur)
2A	Systematic review of cohort studies with homogeneity
2B	Individual cohort study
2C	Ecological studies and "outcomes" research
3A	Systematic review of case-control studies with homogeneity
3B	Individual case-control study
4	Case series or poor quality cohort and case-control studies
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research, or "first principles"

RCT = randomized controlled trial.

REFERENCES

1. Krapohl BD. Functional evaluation of the spine in patients with breast hypertrophy. *Plast Surg Nurs.* 2005;25(4):187-189.

2. Collins ED, Kerrigan CL, Kim M, et al. The effectiveness of surgical and nonsurgical interventions in relieving the symptoms of macromastia. *Plast Reconstr Surg.* 2002;109(5):1556-1566.

3. Chiu TW, Stone C. *Stone's plastic surgery facts and figures.* 3rd ed. Cambridge: Cambridge University Press; 2011.

4. Deyo RA, Mirza SK, Martin BI. Back pain prevalence and visit rates: estimates from U.S. national surveys, 2002. *Spine (Phila Pa 1976).* 2006;31(23):2724-2727.

5. van Tulder MW, Koes BW, Bouter LM. A cost-of-illness study of back pain in The Netherlands. *Pain.* 1995;62(2):233-240.

6. Association APT. "Move Forward" - Low Back Pain Survey. 2012.

7. Ducic I, Iorio ML, Al-Attar A. Chronic headaches/migraines: extending indications for breast reduction. *Plast Reconstr Surg.* 2010;125(1):44-49.

8. Freire M, Neto MS, Garcia EB, Quaresma MR, Ferreira LM. Functional capacity and postural pain outcomes after reduction mammaplasty. *Plast Reconstr Surg.* 2007;119(4):1149-1156; discussion 1157-1148.

9. Mosser SW, Guyuron B, Janis JE, Rohrich RJ. The anatomy of the greater occipital nerve: implications for the etiology of migraine headaches. *Plast Reconstr Surg.* 2004;113(2):693-697; discussion 698-700.

10. Brown AP, Hill C, Khan K. Outcome of reduction mammaplasty--a patients' perspective. *Br J Plast Surg.* 2000;53(7):584-587.

11. Chadbourne EB, Zhang S, Gordon MJ, et al. Clinical outcomes in reduction mammaplasty: a systematic review and meta-analysis of published studies. *Mayo Clin Proc.* 2001;76(5):503-510.

12. Redaelli A, Berjano P, Aebi M. Focal disorders of the spine with compensatory deformities: how to define them. *Eur Spine J.* 2018;27(Suppl 1):59-69.

13. Cano SJ, Klassen AF, Scott AM, Cordeiro PG, Pusic AL. The BREAST-Q: further validation in independent clinical samples. *Plast Reconstr Surg.* 2012;129(2):293-302.

14. Pusic AL, Klassen A, Cano SJ, Kerrigan CL. Validation of the breast evaluation questionnaire. *Plast Reconstr Surg.* 2007;120(1):352-353.

15. Pusic AL, McCarthy C, Cano SJ, Klassen AF, Kerrigan CL. Clinical research in breast surgery: reduction and postmastectomy reconstruction. *Clin Plast Surg.* 2008;35(2):215-226.

16. Mundy LR, Homa K, Klassen AF, Pusic AL, Kerrigan CL. Understanding the Health Burden of Macromastia: Normative Data for the BREAST-Q Reduction Module. *Plast Reconstr Surg.* 2017;139(4):846e-853e.

17. Cerrato F, Webb ML, Rosen H, et al. The impact of macromastia on adolescents: a cross-sectional study. *Pediatrics.* 2012;130(2):e339-346.

18. Ouellet J. Personal Communication. 2018.

19. Berberoglu O, Temel M, Turkmen A. Effects of Reduction Mammaplasty Operations on the Spinal Column: Clinical and Radiological Response. *Aesthetic Plast Surg.* 2015;39(4):514-522.

20. Karabekmez FE, Gokkaya A, Isik C, Saglam I, Efeoglu FB, Gorgu M. Does reduction mammaplasty revert skeletal disturbances in the vertebral column of patients with macromastia? A preliminary study. *Aesthetic Plast Surg.* 2014;38(1):104-112.

21. Sahin I, Iskender S, Ozturk S, Balaban B, Isik S. Evaluation of breast reduction surgery effect on body posture and gait pattern using three-dimensional gait analysis. *Aesthetic Plast Surg.* 2013;37(3):549-553.

22. Lapid O, de Groof EJ, Corion LU, Smeulders MJ, van der Horst CM. The effect of breast hypertrophy on patient posture. *Arch Plast Surg.* 2013;40(5):559-563.

23. Karaaslan O, Demirkiran HG, Silistreli O, et al. The effect of reduction mammaplasty on the vertebral column: a radiologic study. *ScientificWorldJournal.* 2013;2013:701391.

24. Findikcioglu K, Findikcioglu F, Bulam H, Sezgin B, Ozmen S. The impact of breast reduction surgery on the vertebral column. *Ann Plast Surg.* 2013;70(6):639-642.

25. Barbosa AF, Lavoura PH, Boffino CC, et al. The impact of surgical breast reduction on the postural control of women with breast hypertrophy. *Aesthetic Plast Surg.* 2013;37(2):321-326.

26. Tenna S, Brunetti B, Trivelli M, Salvinelli F, Persichetti P. Postural variations after breast reduction: introduction of a new technique to achieve an objective analysis. *Ann Plast Surg.* 2012;68(3):261-264.

27. Foreman KB, Dibble LE, Droge J, Carson R, Rockwell WB. The impact of breast reduction surgery on low-back compressive forces and function in individuals with macromastia. *Plast Reconstr Surg.* 2009;124(5):1393-1399.

28. Benditte-Klepetko H, Leisser V, Paternostro-Sluga T, et al. Hypertrophy of the breast: a problem of beauty or health? *J Womens Health (Larchmt).* 2007;16(7):1062-1069.

29. Coltman CE, Steele JR, McGhee DE. Breast volume is affected by body mass index but not age. *Ergonomics.* 2017;60(11):1576-1585.

30. Papanastasiou C, Fortin M, Ouellet J, Lessard L. PSRC Podium Presentation & Abstract QS 36: Quantitative Orthopaedic Spine Benefits Post Breast Reduction - Preliminary Results. *Plastic and Reconstructive Surgery.* 2018;6(4S):138.

31. Kerrigan CL, Collins ED, Kim HM, et al. Reduction mammaplasty: defining medical necessity. *Med Decis Making.* 2002;22(3):208-217.

32. Kerrigan CL, Collins ED, Striplin D, et al. The health burden of breast hypertrophy. *Plast Reconstr Surg.* 2001;108(6):1591-1599.

33. Cabral IV, Garcia ED, Sobrinho RN, et al. Increased Capacity for Work and Productivity After Breast Reduction. *Aesthet Surg J.* 2017;37(1):57-62.

34. Statcan. Statistics Canada - Overweight and obese adults (self-reported), 2014. 2014.

35. Gonzalez MA, Glickman LT, Aladegbami B, Simpson RL. Quality of life after breast reduction surgery: a 10-year retrospective analysis using the Breast Q questionnaire: does breast size matter? *Ann Plast Surg.* 2012;69(4):361-363.

RATIONALE FOR SYSTEMATIC REVIEW AND PROSPECTIVE COHORT STUDY

Before undertaking this in-depth back pain / breast hypertrophy prospective cohort study, it was crucial to first examine the literature related to this research domain. As such, a comprehensive systematic review was carried out and published by our group.[35] Our objective was to integrate the literature on breast hypertrophy, back pain, breast reduction, and its effects on the spine. The specific focus was to find and analyze, in the best quantitative manner, radiological studies and those investigating changes in posture, center of gravity, spinal angles, and pain reduction. Many of the studies found were only qualitative in nature or too small.

This review served two purposes. Out of an initial search result of 107 articles, only 11 final articles were chosen after applying inclusion and exclusion criteria. These articles provided us with a good summary of the limited literature on reduction mammaplasty, related pain, and the spine. Secondly, it exposed an important lack of knowledge in this area of research. The conclusion drawn from our review of the literature was that even today, there is a lack of understanding of breast hypertrophy, back pain, and its negative effects on the spine. A strong need for further research was recognized, particularly with enhanced quantitative methodology and technology.[29, 35, 36]

Chapter 2: Breast Hypertrophy – A Real Pain in The Back

Abstract (Eng)

Background

Breast hypertrophy comes with an array of signs and symptoms that range from mild to debilitating in nature including neck and upper back pain, aching shoulders, painful shoulder grooves, low back pain, intertrigo of the inframammary crease, mastalgia, poor posture, and difficulty with exercise. Breast reduction surgery is one of the most frequently performed plastic surgery procedures that has been shown to have the highest patient satisfaction and improvement in quality of life on specific satisfaction survey questionnaires. The effects of breast reduction surgery on parameters such as spinal balance, paraspinal muscle function, and physical performance have not been thoroughly evaluated. The objective of this prospective study is to evaluate the effects of reduction mammaplasty on spinal balance, paraspinal muscles, and physical function using sophisticated spine surgery imaging modality pre and post breast reduction, as well as pain resolution.

Methodology

A prospective, observational cohort study was carried out at the Montreal General Hospital (MGH) of the McGill University Health Centre (MUHC). Twenty-

five patients were being prospectively enrolled in this IRB approved study. The following outcome measures were recorded preoperatively and postoperatively for each patient: Clinical evaluation, patient self-assessment outcomes including Breast-Q (validated questionnaire in French & English), MRI of the spine, and EOS X-ray (ultra-low dose radiation) of the spine in standing position.

Results

Significant postoperative pain reduction and up to 119% improvement in physical tests. Postoperative improvement in thoracic kyphosis was documented quantitatively on patients scanned in the standing position. Improvement in all Breast-Q categories documented. Preoperative and postoperative MRI of the spine demonstrate no wear and tear which was statistically significant.

Conclusion

Reduction mammaplasty is a procedure with quantitative morphological spine benefits. This additional benefit may have an impact on health care system and third-party payer insurance companies and may beckon the need for more precise guidelines based on those quantitative findings.

ABSTRACT (FR)

Contexte

L'hypertrophie mammaire s'accompagne d'un éventail de signes et de symptômes allant de légers à débilitants de nature, y compris des douleurs au cou, aux épaules et au haut du dos, des sillons douloureux aux épaules, des douleurs au bas du dos, de l'intertrigo du pli inframammaire, de la mastalgie, une mauvaise posture et de la difficulté à faire de l'exercice. La chirurgie de réduction mammaire est l'une des interventions de chirurgie plastique les plus fréquemment pratiquées, qui a démontré les meilleurs résultats au niveau de la satisfaction des patientes et de l'amélioration de leur qualité de vie selon certains questionnaires d'enquête sur la satisfaction. Les effets de la chirurgie de réduction mammaire sur des paramètres tels que l'équilibre rachidien, la fonction musculaire paraspinale et la performance physique n'ont pas été soigneusement évalués. Ainsi, l'objectif de cette étude prospective est d'évaluer les effets de la réduction mammaire sur l'équilibre rachidien, les muscles paraspinaux et la fonction physique à l'aide de techniques sophistiquées d'imagerie utilisées lors des chirurgies de la colonne vertébrale, avant et après la réduction mammaire, ainsi que la réduction de la douleur.

Méthodologie

Une étude de cohorte prospective et observationnelle a été réalisée à l'Hôpital général de Montréal (HGM) du Centre universitaire de santé McGill (CUSM). Vingt-cinq patientes étaient inscrites prospectivement à cette étude approuvée par la CISR. Les mesures de résultats suivantes ont été enregistrées avant et après l'intervention pour chaque patiente : un rayon-X EOS (ultra-faible dose de rayonnement) de la colonne vertébrale en position debout, une IRM de la colonne vertébrale, une évaluation clinique, ainsi qu'une autoévaluation de la patiente, comprenant le questionnaire Breast-Q (questionnaire validé en français et en anglais).

Résultat

L'amélioration postopératoire de la kyphose thoracique a été documentée quantitativement sur les patientes scannées en position debout. Les IRM préopératoire et postopératoire de la colonne vertébrale ne montrent aucune usure. Il y a eu une réduction importante de la douleur postopératoire et une amélioration jusqu'à 119 % au niveau des tests physiques, ainsi qu'une amélioration documentée dans toutes les catégories du Breast-Q.

Conclusion

La réduction mammaire offre une amélioration quantifiable de l'alignement de la colonne vertébrale et de la réduction de la douleur au cou et au dos. Cet avantage supplémentaire pourrait avoir une incidence sur le système de santé et les sociétés d'assurances, et peut mettre en évidence la nécessité d'instaurer de meilleures lignes directrices fondées sur ces constats quantitatifs.

CONTRIBUTION OF AUTHORS

Constantine Papanastasiou, MD, MSc(c) - first author, data acquisition & analysis

Maryse Fortin PhD – co-author, MRI analysis

Jean A. Ouellet, MD, FRCSC – co-author, orthopedic EOS collaboration

Lucie Lessard MD, FRCSC, FRCSC, FACS – Senior author, concepts and idea, principal investigator, and corresponding author

BACKGROUND

Breast hypertrophy comes with a vast array of signs and symptoms that range from mild to debilitating in nature. The most common physical complaints associated with breast hypertrophy include neck and upper back pain, aching shoulders, painful shoulder grooves, low back pain, intertrigo of the inframammary crease, mastalgia, poor posture, and difficulty with exercise. [1-3] The pathophysiology of breast hypertrophy-induced back pain and the above signs and symptoms can be quite severe requiring chronic use of analgesic medications around the clock. Correlations have even been reported between macromastia, shoulder and upper extremity pain, and carpal tunnel syndrome in the most severe cases. [37] Breast hypertrophy also has a significant negative impact on the self-esteem and health-related quality of life of affected females.[16]

Breast hypertrophy can present as classic macromastia or virgin gigantomastia which are the usual two related conditions in which the breasts attain excessive size and volume. Large breasts that do not exceed a mass of 2.5 kg per breast characterize macromastia. [3] Other types of breast hypertrophy include: hypertrophy of infancy, gestational hypertrophy, breast hypertrophy of extreme obesity, and drug-induced breast hypertrophy.[3, 38, 39]

Breast hypertrophy is caused by the excessive hyperplasia of fatty and glandular tissue.[40] It has been suggested that hypersensitivity to elevated hormone levels and or increased expression of hormone receptors can cause macromastia. Some of these hormones include estrogen, progesterone, hepatocyte growth factor (HGF), and prolactin.[40-42] In cases of juvenile breast hypertrophy, breast tissue typically shows varying degrees of stromal and ductal hyperplasia with dilatation of ducts. Collagenous fibrosis and cellular myxoid hyperplasia can sometimes be seen.[43] However, at present, none of these etiologies can be controlled with medical treatment. The sole option is still surgical, consisting of partial resection of breast tissue while maintaining an adequate breast shape.

Typically, patients seek reduction mammoplasty when they have some or all of the following symptoms: neck pain, shoulder pain, back pain, breast pain and painful grooves.[44] The purpose of breast reduction surgery is to reverse pain while achieving smaller breasts, aesthetic shape, symmetry, and less volume.[3] Reduction mammaplasty has a high patient satisfaction rate.[9] Previous Breast-Q studies revealed that over 95% of patients were pleased postoperatively and 96% of those would “do it again”[34] The cause of their spinal pain remains somewhat poorly understood as do the reasons for the resolution of their pain. It is thought that the change in center of mass changes the spinal alignment which alleviates patients’ aberrant muscular compensation.

There are two main surgical techniques used today: the Inverted T – horizontal technique with inferiorly based dermocutaneous flap; and the newer vertical technique with a superior or superomedial flap and short vertical scar.[3] All our patients were operated with the latest technique, preferred surgical technique of the senior author. Vertical scar mammaplasty is the technique of choice for many plastic surgeons and has been popularized by several prominent surgeons over the past 20 years.[45-48] It is a technique that results in reduced scarring, more upper pole fullness, and less bottoming out.[3] It results in a breast that ages better with time.[48] The technique uses a superomedial dermal pedicle. [49]

General complications may include infection, hematoma, dehiscence, scarring, DVT/PE. More specific complications of reduction mammoplasty include asymmetry/under- or over-correction, nipple loss, change in nipple sensation, fat necrosis, dog ears, and scar hypertrophy.[3, 45]

A better understanding of spinal anatomy and spinal posture is essential to identify the effect of mammaplasty as it impacts neck and back pain resolution. The spine is divided into seven cervical, twelve thoracic, five lumbar, five fused sacral, and four fused coccygeal vertebrae, for a total of 33 vertebrae. Powerful paraspinal muscles, intervertebral discs, tendons, and ligaments all contribute to the ability to maintain an upright position. From the lateral perspective, the spine has a natural S-shaped curve with classic cervical lordosis, thoracic kyphosis, and lumbar lordosis enabling the spine to absorb shock and distribute forces.

This delicate balance can be disrupted altering the physiological curves leading to different pathologies and conditions. For example, the excessive mass of the breasts pulls down the fascial sling surrounding the shoulders and neck. This traction on the trapezius and muscles of the posterior neck has been shown to cause pressure on the greater occipital nerve, lesser occipital nerve, and dorsal occipital nerves. Previous authors have also reported a decrease in headaches after breast reduction.[6] Breast hypertrophy can even cause increased compressive forces in the lower spine. [26] Certain studies have demonstrated that breast volume has a direct correlation to posture, thoracic kyphosis angle, and lumbar lordosis.[22] "Breast hypertrophy causes the geometric location of the center of gravity to move upward and forward and leads to the need for postural compensation and adjustments. These adjustments attempt to equilibrate the body mass distribution (e.g., by increasing the tonus of the posterior muscles), and these changes may cause significant postural alterations, such as exacerbation of the spine's curvature or an increase in the tension of the cervical extensor muscles." [24] The well-balanced spine stays upright using the minimal level of energy expenditure possible. The mass of hypertrophic breasts acts to upset steadying forces of the back and neck. The body's center of gravity is subsequently altered. This center of gravity moves anteriorly and superiorly. The outcome is a distorted spine curvature with augmented cervical lordosis, thoracic kyphosis, and lumbar lordosis. This results in contraction of the paraspinal muscles which acts to compensate for the change in spine curvature. Often the pain is so severe, patients rely on chronic pain control medication around the clock with minimal success to have any sort of quality of life.[11]

Our primary motivation for this study was to confirm that breast hypertrophy did indeed lead to the described abnormal spinal alignment and the maladaptive muscle compensation described by Redaelli et al.[11] This was accomplished by quantifying validated outcome measures pre and postoperatively, specifically on spinal alignment. The first objective was to evaluate the effects of breast reduction surgery on sagittal balance, change in center of gravity, and spinal pain. This has never been done with the technology proposed. Breast reduction mammaplasty has been shown to result in a very high patient satisfaction rate, often as high as 95%.[34] The improvement in quality of life, self-esteem, as well as physical and psychological benefits following surgery has been well documented.[2, 50, 51] Nevertheless, these findings are based on patient perception based on validated questionnaires. Although some recent studies have attempted to use more objective measures to assess changes in patient posture post-surgery (e.g. spine x-rays,[19, 22, 23] postural control,[21, 24] gait analysis[20]), results are conflicting. Only five previous studies compared reduction mammaplasty patients' preoperative and postoperative spinal angles with older technology and never with EOS.[18, 19, 21-23]

Considering that muscle function can be correlated with muscle mass, we felt it was important to investigate the quantitative effects of breast reduction surgery on paraspinal muscle size and composition by using MRI.[52] It has been suggested that heavy breasts can increase cervical lordosis and thoracic kyphosis, by shifting the center of gravity away from the spine, which increases the muscular effort needed to maintain balance, and in turn leads to continuous tension on the trapezius (middle and lower fibers) and associated muscle groups.[53] Although the musculoskeletal system is clearly affected in women with breast hypertrophy, very few studies[54] have investigated the effect of breast hypertrophy on muscle. The functional benefits of breast reduction mammaplasty on the musculature deserve further attention.[29, 35, 36]

The second aim of the study was to quantify the effects of breast reduction mammaplasty on overall quality of life and pain levels. The controversy related to the efficacy of breast reduction mammaplasty exists because the literature supports the theory that this surgical procedure improves the clinical signs and symptoms associated with breast hypertrophy but there is a lack of quantitative studies in the literature specific to back pain.

Finally, the third aim was to clarify the impact of breast reduction surgery on physical activity. Patients often report subjective improvement in their level of activity, the intent of the third aim was to quantify their physical activity pre and postoperatively.

Knowing that pain is multifactorial, improvement in self-image and easier time exercising could all influence the overall symptomatic relief of pain. To the best of our knowledge, there are no studies that have quantitatively assessed the relationship between breast reduction surgery, physical activity, and pain relief.

The first hypothesis is that women with breast hypertrophy have abnormal sagittal spinal alignment and may have increased incidence of degenerative changes of the vertebra and intervertebral discs. The second hypothesis is that that breast reduction mammaplasty will significantly alter spinal alignment for the better. The third hypothesis is that breast reduction mammaplasty will reduce or alleviate back pain and improve physical activity.

METHODOLOGY

This is a prospective cohort study, carried out at the Montreal General Hospital (MGH) and Royal Victoria Hospital (RVH) of the McGill University Health Centre (MUHC).

Sample size estimation and prior data collection showed a 2.7 (SD=4.8) difference in the mean response of matched pairs for thoracic kyphosis angle, and 3.3 (SD=4.6) for lumbar lordosis angle following breast reduction surgery.[23]

Accordingly, a total of 25 subjects were needed for a comparison of the thoracic kyphosis angle and 16 for lumbar lordosis angle in order to reject the null hypothesis of zero difference between pre- and post-surgery spinal angles (power of 0.8 and alpha of 0.05). Thus, the aim was to recruit a total 25-30 patients undergoing breast reduction surgery. Sample-size estimation was performed using Stata (version 12.0; StataCorp LP, College Station, TX, USA). The recruitment period spanned 2 years. Each patient was followed for a total of 6 months.

The inclusion criteria were: female patients with breast hypertrophy, aged 18 to 70 years old. Patients were required to have back pain. Breast reduction for all study patients was planned and performed by the same senior plastic surgeon. A minimum reduction of 250 grams per breast was performed (health care system minimum for coverage), as well as informed consent. The exclusion criteria were pregnancy, prior spine surgery, prior breast reduction surgery, spinal pathology, or systemic disease. Aesthetic mastopexy patients were also excluded. In addition, patients who met the withdrawal criteria included those who had spinal trauma or became pregnant during the study.

All patients who met the inclusion criteria were approached by the research team and an informed consent was obtained. The subjects were recruited through the MGH and RVH plastic surgery outpatient adult clinic and were patients referred to the senior plastic surgeon. Surgery and all follow-up visits took place at the MGH and RVH. Outcome measures were collected as outlined in the master schedule (See Table 1). The physiotherapy assessments were performed on the same day as the EOS images. MRI imaging was carried out at the MGH as outlined in the master schedule. (See Table 1)

To the best of our knowledge, this study is the first in the world to use EOS for spine evaluation on breast reduction patients. EOS is not an acronym; it is the proper name of this imaging technology that is used for scoliosis assessments of patients before and after spine surgery. The major advantage of EOS is a very low radiation exposure for the patients at a level up to 85% lower for spine radiographs than standard radiology imaging.[55] Moreover, due to superior images of bones structures, EOS 3-D imaging allows for better evaluation of the center of gravity and sagittal balance. EOS bursts expose a patient to about 0.22 mGy - 0.60 mGy of irradiation.[55, 56] The EOS images are used to provide critical 3D information on spinal alignment from a standing position. MRI documentation, on the other hand, is not presently available in the standing functional position.

In our methodology, MRI images are collected to rule out any significant spinal pathologies pre-surgery and evaluate the effects of breast hypertrophy on paraspinal muscle size and quality. Cross-sectional area (CSA) and functional cross-sectional area (FCSA) of the paraspinal musculature were analysed.

Patient clinical assessments were carried out at four visits: initial visit, 2 weeks postoperative, 6 weeks postoperative, and 6 months postoperative. At the initial visit, after patients were recruited and consented, they were requested to complete the following self- assessment questionnaires: McGill Pain Questionnaire, Visual Analogue Scale (VAS) and Pain Diagram, Pain Catastrophizing Scale (psychological response to pain), Oswestry Disability Index, Short-Form 12 (SF-12), and Breast-Q. Additionally, the following clinical and physiotherapy evaluations were conducted: calculation of BMI, physical performance measures (5X sit to stand test, stair climbing, and Sorensen core test) [10]. The imaging that took place at the initial visit included an EOS image as well as magnetic resonance imaging (MRI). (See Figure 9)

On the day of surgery, resection weight was documented. Two days postoperatively patients were seen for dressing change, drains were never used. Two weeks postoperatively, the patients were seen by the senior plastic surgeon and the MSc student for a follow-up visit to ensure proper wound care and dressings. The patients were also asked to complete the same set of self-assessment questionnaires.

At postoperative week 6, patients completed the self-assessment questionnaires, underwent the clinical and physiotherapy evaluation and testing, and were sent for their postoperative EOS images of the spine.

The final patient visit took place 6 months postoperatively. At this time point, patients were seen by the senior plastic surgeon and the MSc student, completed a final set of self-assessment questionnaires, and underwent a postoperative MRI. The analyses were performed on the data based on 25 patients. Pre-surgical values were subtracted from the post-surgical ones to obtain the change in each score (delta). Positive change values mean that the post-surgical value increased, while negative values indicate the opposite. Data are expressed as the mean and standard deviation. Statistical analysis was performed using the statistical package R v.3.3.2 and Rstudio v1.0.153.

Comparison between pre and post-surgical values was performed using paired t-tests. Correlation between variables was assessed through linear regression. Statistical significance was set at a p value of <0.05.

RESULTS

A total of 25 women with back pain and breast hypertrophy with various breast sizes were evaluated in this study. Patients ranged from 18 to 71 (mean of 41 $\pm$ 7.2) years of age. Mean BMI for the patient cohort was 28.3. Two patients (8%) had a "normal" BMI value between 18.50-24.99, 15 patients (60%) were "overweight" (BMI 25.00-29.99), and eight patients (32%) were "obese" (BMI > 30.00). In terms of preoperative breast cup size, 1 patient had G cups, 2 patients had E cups, 7 patients had DD cups, 10 patients had D cups, and 5 patients had C cups but had severe back pain.

A statistically significant difference between preoperative and postoperative neck, back, and lumbar pain were demonstrated by the VAS (mean reduction in pain value -3.44 ($p < 0.001$)) -34%, McGill Pain Questionnaire (mean reduction in pain value -9.32 ($p < 0.001$)) -21%, and Pain Catastrophizing Scale (mean reduction in pain value -21.36 ($p < 0.001$)) -42%. No statistically significant correlation was found between resected mammary mass and pain reduction. (See Figure 1)

The Oswestry Disability Index demonstrated a statistically significant mean reduction in disability due to back pain of -11.68 ($p < 0.001$) postoperatively. Lastly, the SF-12 questionnaire demonstrated an improvement of 6.22 ($p = 0.001$) in overall health-related quality of life. (See Figure 2 and Figure 9)

The Breast-Q satisfaction questionnaire revealed a statistically significant postoperative improvement in all categories including breast satisfaction (mean increase in score of 46.5 ($p < 0.001$)), psychosocial well-being (mean increase in score of 37.5 ($p < 0.001$)), sexual well-being (mean increase in score of 35.3 ($p < 0.001$)), and physical well-being (mean increase in score of 23.4 ($p < 0.001$)).

(See Figure 3)

When comparing pre- and postoperative physical performance measures, a statistically significant difference was demonstrated by the stair climbing test (mean increase in flights stairs of 1.82 ($p < 0.001$)) 17% improvement, Sorensen core test (mean increase in plank time of 27.69 seconds ($p < 0.001$)) 119% improvement, and the 5X sit-to-stand test (mean improvement in time of 1.42 seconds ($p = 0.02$)) 19% improvement. (See Figure 4 and Figure 9)

In terms of MRI analysis comparing pre- and postoperative cervical and thoracic levels of the spine, there were no statistically significant changes in cross-sectional area or functional cross-sectional area and no significant evidence of excess spinal wear and tear of any of the tissues.

(See Figure 5)

With respect to spinal alignment and spinal balance using EOS imaging, a statistically significant difference between pre- and postoperative thoracic kyphosis angles was found. T1/T12 thoracic kyphosis improved by nearly 5 degrees ($p < 0.001$) and T4/T12 thoracic kyphosis demonstrated an improvement of over 4 degrees ($p = 0.001$). (See Figure 6 and Figure 9)

DISCUSSION

In the context of our prospective study, it was essential to examine the patients using a multimodalities approach. The final methodology was to collect comprehensive data via multiple validated pain and disability questionnaires (eg. VAS, McGill Pain Questionnaire, and pain catastrophizing scale), physical capacity testing, MRI, and EOS. This approach ensured that patient data was all-inclusive to assess spine changes thoroughly and in-depth.

It is known that breast hypertrophy causes severe pain for patients. Our study made use of four validated pain questionnaires which were completed by patients at multiple time points both pre- and postoperatively (See Table 1). A statistically significant reduction in pain and disability were demonstrated by all of these measures. These results are consistent with our systematic literature review, whereby studies that applied a component of pain evaluation demonstrated a significant improvement in pain postoperatively.[24] Clinically, our group repeatedly noted that postoperative pain alleviation for the patient cohort was rather immediate and instantaneous and not gradual in time frame. Postoperatively, patients were already subjectively relieved of back pain in the PACU, and a mere 2 weeks after surgery, back pain questionnaires were already being scored at their best final values, similar to their results at 6 months post-op mark. Analysis of data showed no statistically significant association between resected mammary mass and pain reduction. Patients who had undergone the minimum breast reduction of

250 grams were objectively and subjectively as relieved of pain as those patients who had larger reductions in the 1000 gram range. We were fascinated and perplexed that even a 250 gram volume reduction per breast resolved back pain clinically in several patients. This study can provide important feedback to health care systems in that even a 250 gram resection relieves pain significantly.

In addition to physical disturbances, breast hypertrophy has a significant negative impact socially, psychologically, and as it relates to self-esteem and health-related quality of life of patients. The improvement in quality of life, self-esteem, as well as the physical and psychological benefits following surgery has been well documented.[2, 50, 51 15, 57] To ascertain and quantify quality of life, patients in this study were asked to complete the state-of-the-art validated Breast-Q and Short Form 12 (SF-12) both pre- and postoperatively.[12-15] All questionnaires were available in both English and French. Statistically significant postoperative improvements were determined for all categories including satisfaction with breasts (47% improvement), psycho-social well-being (39% improvement), sexual well-being (38% improvement), and physical well-being (25% improvement). This is consistent with previous Breast-Q studies, which revealed that over 95% of patients were pleased post breast reduction and 96% of those would “do it again”.[15, 34, 50] The SF-12 offers insight into a patient’s overall health-related-quality of life. It was determined that there were statistically significant improvements in both postoperative SF-12 physical composite scores and mental composite scores for our cohort. This is an excellent indication of improvement in quality of life postoperatively as the SF-12 is weighted and summed to provide easily interpretable scales for physical and mental health.[58]

For most breast hypertrophy patients, the combination of back pain, altered center of gravity, and clothing/bra discomfort make exercise a substantial challenge. In order to quantifiably assess the capacity for exercise in this prospective study, standardized physical therapy (PT) tests were carried out pre- and postoperatively on all patients including the 5X sit-to-stand test, stair climbing test, and Sorensen test (plank exercise for assessing trunk extensor muscles and core strength). The 5X sit-to-stand test measures functional lower extremity strength, transitional movements, balance, and fall risk.[59] The stair climbing test assessed patients' cardiovascular capacity. It is worth noting that the Sorensen test demonstrated a drastic improvement in plank time of 119% postoperatively. The results indicated statistically significant improvements in physical performance in all three standardized physical tests. Breast hypertrophy is a disabling condition that limits a patient's capacity for physical activity.[34, 54, 57] Our results demonstrated that postoperatively, breast reduction surgery resulted in more active and more physically performant patients.

For this technical and in-depth study, MRI was used both pre- and postoperatively on all of our patients. The size and composition of the cervical and thoracic paraspinal muscles were assessed using a quantitative and highly reliable validated MRI method developed by one of our co-authors.[60] (See Figure 7) The results of the MRI analysis revealed no statistically significant change in paraspinal muscle size and quality. Interestingly, after a thorough analysis, we could conclude that there was also no wear and tear of the vertebra or its intervertebral discs. In several of these patients, despite decades of chronic back pain, there were no signs of anatomical anomalies nor accelerated degeneration. The severe pain associated with breast hypertrophy is totally reversible post breast reduction. It is not associated with any permanent damage, but is due instead to abnormal posture, also reversible post breast reduction.

This finding may illustrate that patients' pain may be secondary to functional changes in muscle tension and fatigue, rather than classic back pain etiologies like static abnormalities. Classic etiologies include disc degeneration and facet arthritis. In the case of breast hypertrophy, patients' neck and back pain is comparable to muscle fatigue, the result of muscular compensation for the abnormal anterosuperior weight distribution. As this weight is removed, the muscle no longer needs to work continuously and thus the patients are finally in a better resting phase.

In addition to positive results in pain questionnaires, satisfaction surveys, physical testing, and MRI, our prospective study is the first in the world to use EOS. (See Figure 8 and Figure 9) EOS enables accurate 3D reconstruction of the spine in the standing position, isolating each vertebra and carrying out angle calculations within its software.[61] It is an image that is a true 3D representation of the spine that is highly accurate and highly reproducible. It is of great use for adolescent idiopathic scoliosis assessments clinically and in research.[62, 63] The previous studies used regular first generation spine x-rays and results between them were conflicting.[35] None of them used EOS and we offer this prospective study using this advanced technology. EOS imaging is done in the standing position which is clinically the most painful position for breast hypertrophy patients.

EOS was used in this study to assess spinal angle changes in breast reduction patients experiencing back pain. Our EOS results are consistent with our hypothesis that postoperatively, there will be a decrease in thoracic kyphosis reflecting a shift of center of gravity, resulting in less muscle strain to stay upright, and thus less back pain.[24] The association between abnormal posture and back and neck pain is widely accepted in the literature.[64-66] A neutral spine maintains a neutral equilibrium using the minimum energy expenditure possible. The final results indicate a significant improvement in both T1/T12 and T4/T12 thoracic kyphosis. T1/T12 thoracic kyphosis improved by 5 degrees ($p < 0.001$) and T4/T12 thoracic kyphosis improved by 4 degrees ($p = 0.001$). Improved thoracic kyphosis angles were also described in previous radiological studies, although they used ordinary first generation xrays.[18, 19, 23] EOS offers superior accuracy of +/- 1 degree, compared to less accurate plain x-rays which ranged in imprecision up to +/- 6 degrees. Hypertrophic breasts and their excessive mass on the chest act to upset the forces on the neck and back. The patient's center of gravity is thus shifted anterosuperiorly. In breast hypertrophy, the outcome is a spine with exaggerated thoracic kyphosis. There is also an additional compensatory contraction of the paraspinal muscles which can result in major and consistent back pain. Patients often require chronic pain control medication just to get through the day. Breast reduction causes a decrease in thoracic kyphosis, reflecting a shift of center of gravity posteriorly. This results in less muscle strain to stay upright, and thus less pain. [11] Combined with our MRI results which refute the wear and tear possibility, this is an encouraging result for our breast hypertrophy patients considering surgery. Plastic surgeons can thus guide and instruct breast hypertrophy patients safely with regards to back pain resolution and the positive surgical outcome.

Patients with breast hypertrophy often required chronic pain control medication just to get through the day. Breast reduction gives these patients hope to reverse this back pain in 95% of cases, and without any permanent damage. EOS confirmed a reversion to a more neutral posture. Capacity for exercise improved by up to 119% in our physical therapy assessments. Our quantitative MRI methodology did confirm the absence of wear and tear in breast hypertrophy patients, and points to the possibility of a major quality of life improvement postoperatively.

Tables and Figures

Table 1: Master schedule - outcome measures recorded at different time points

		Initial Visit	1-2 weeks post-op	6 weeks post-op	6 months post-op
	Consent/Screening	X			
Questionnaires (ENG & FR)	Visual Analogue Scale (VAS)	X	X	X	X
	McGill Pain Questionnaire	X	X	X	X
	Pain Catastrophizing Scale	X	X	X	X
	Oswestry Disability Questionnaire	X	X	X	X
	SF-12	X	X	X	X
	Breast-Q	X	X	X	X
Plastic Surgeon	Plastic Surgery Post-Op Follow-Up	X	X	X	X
Physical Assessments	5x Sit-To-Stand Test	X	X	X	X
	Stair Climbing Test	X	X	X	X
	Sorensen Test	X	X	X	X
Imaging	MRI	X			X
	EOS	X		X	

Figure 1: Pain Questionnaires Results

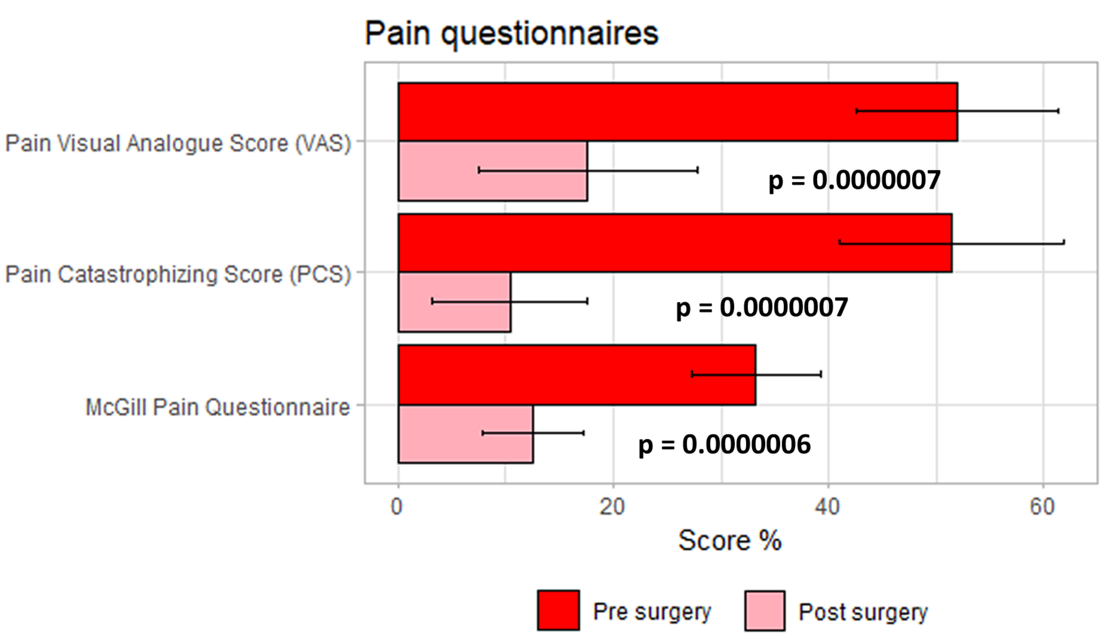


FIGURE 2: DISABILITY AND QUALITY OF LIFE QUESTIONNAIRES RESULTS

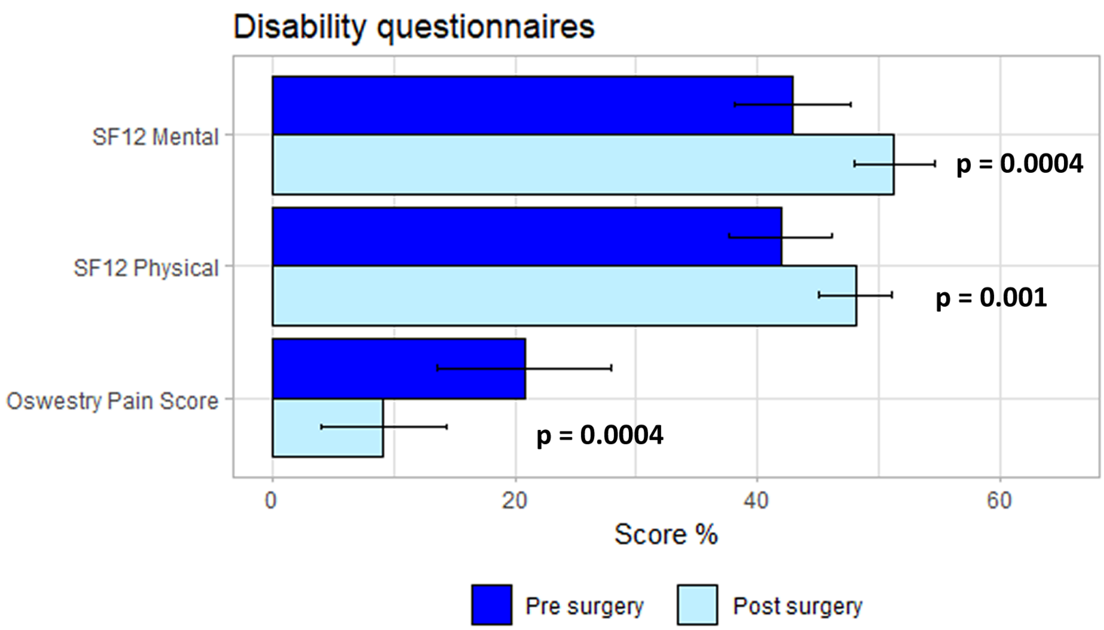


FIGURE 3: BREAST-Q QUESTIONNAIRE RESULTS

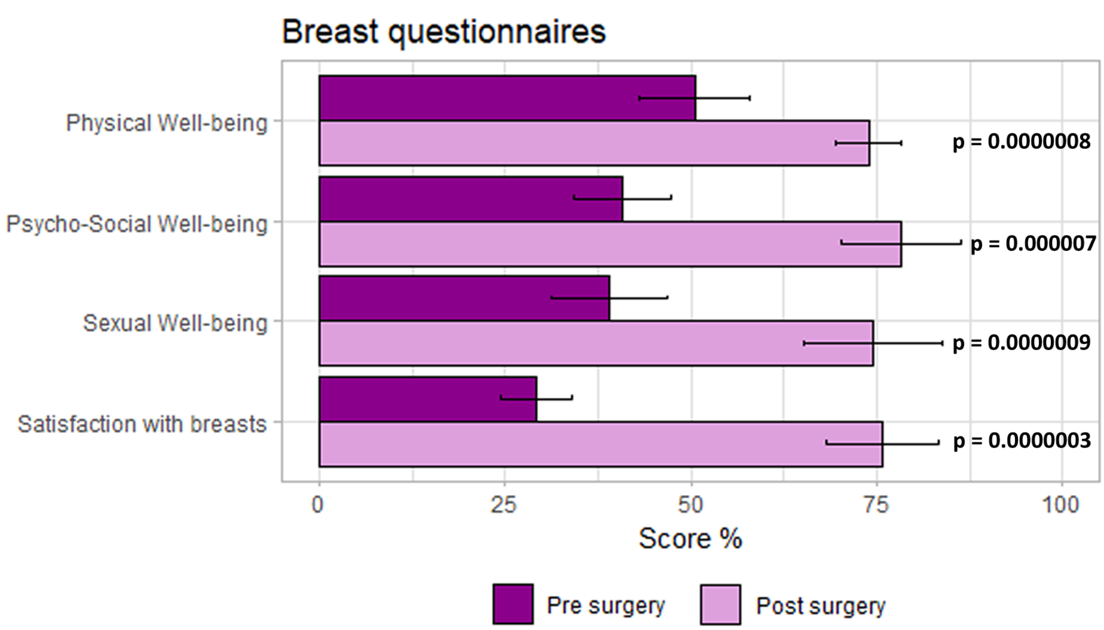


FIGURE 4: PHYSICAL TESTING RESULTS

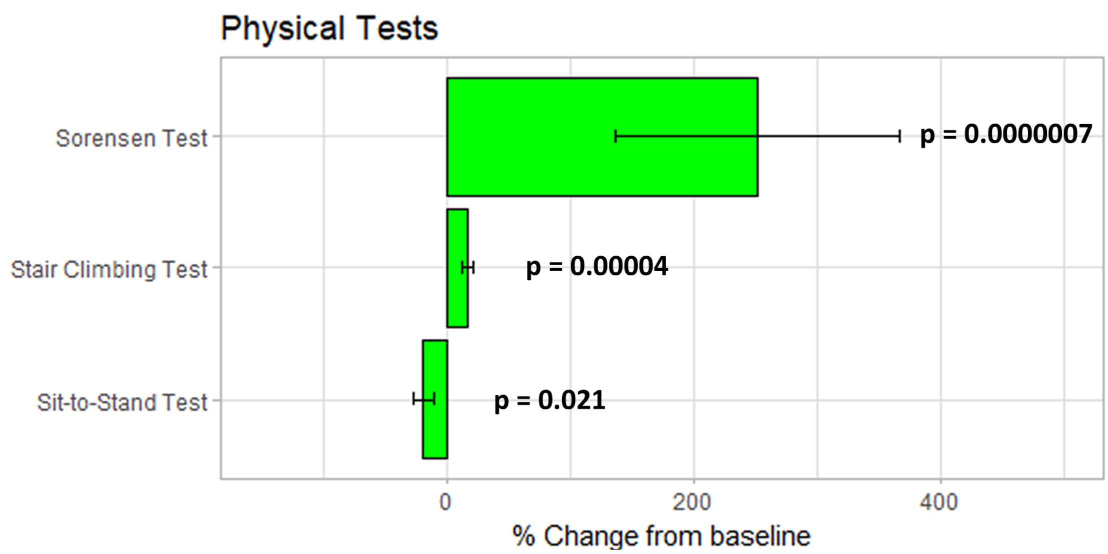


FIGURE 5: MRI RESULTS

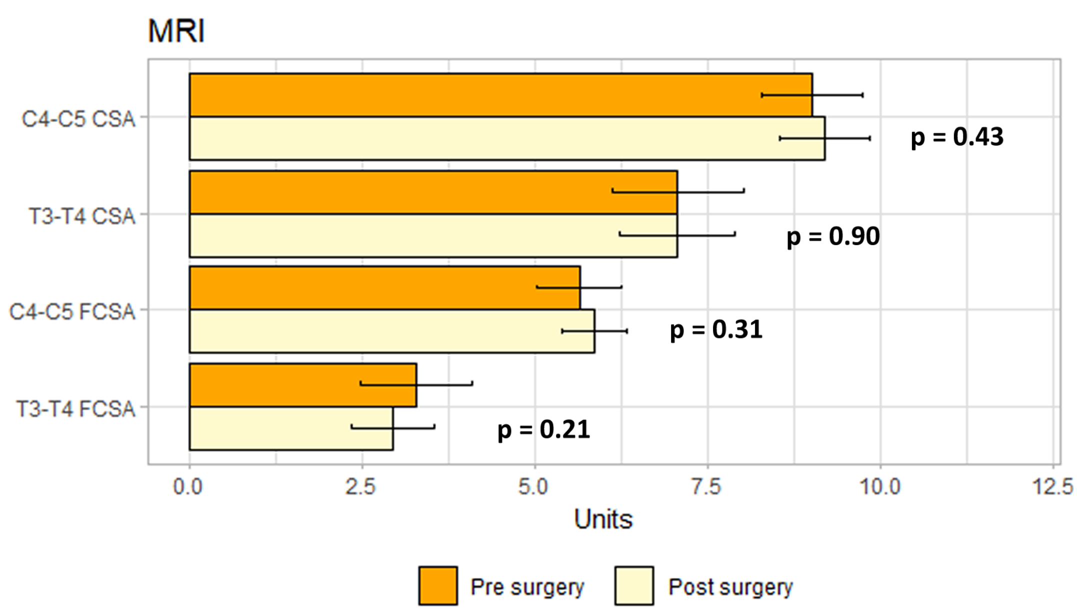


FIGURE 6: EOS RESULTS

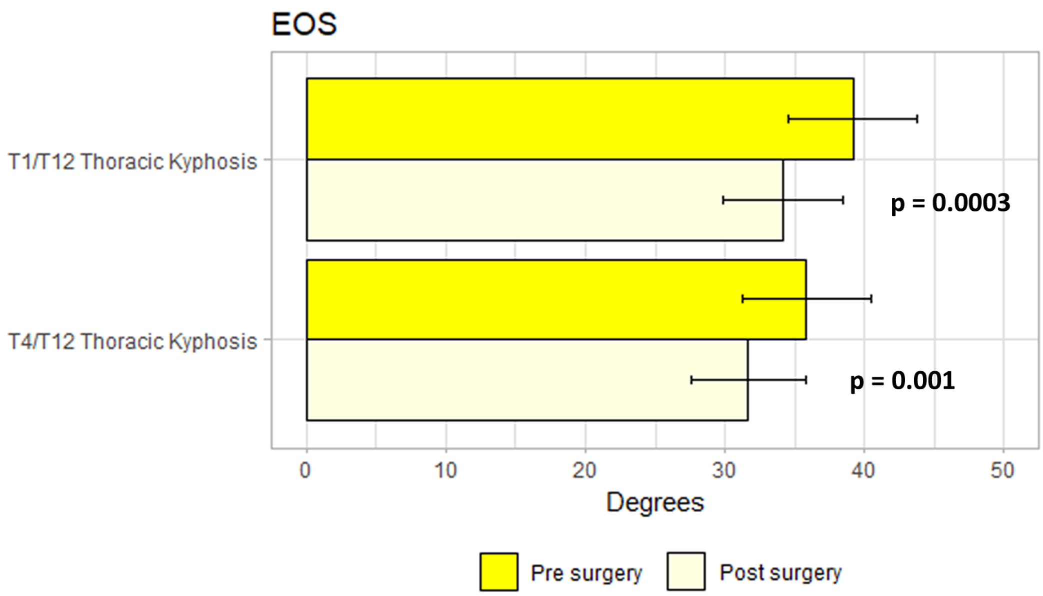


FIGURE 7: MRI CROSS-SECTIONAL AREA TECHNIQUE

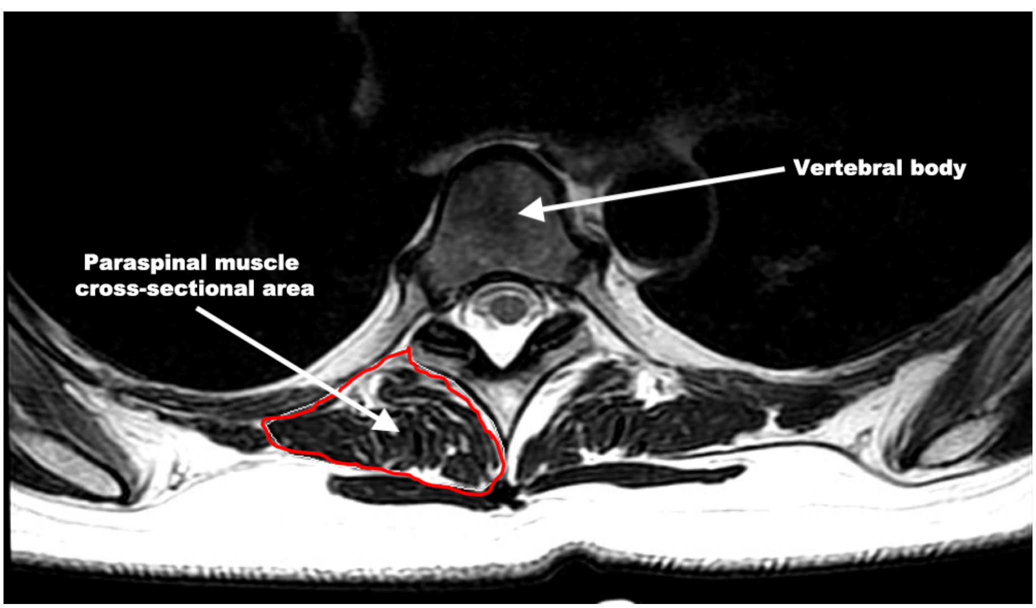
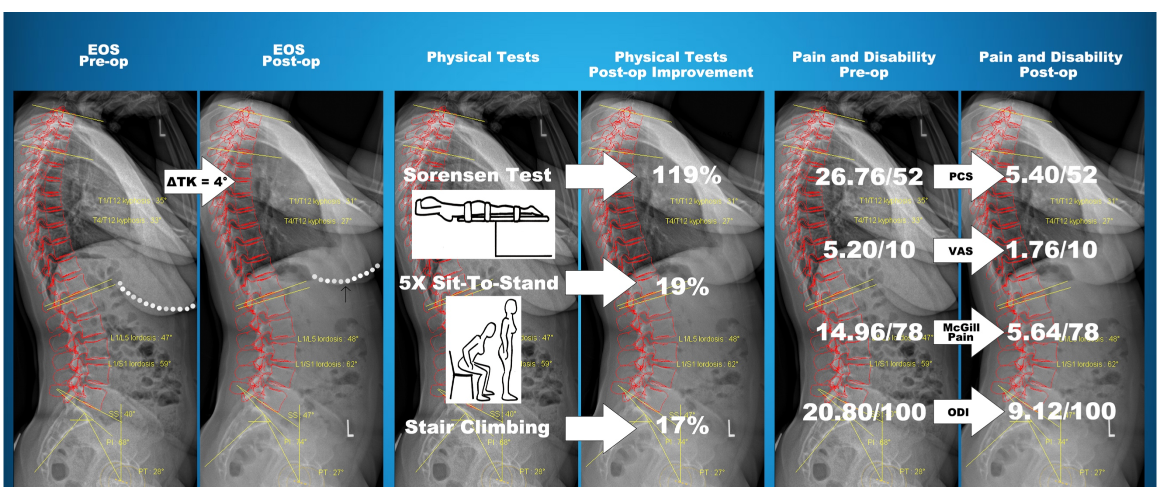


Figure 8: EOS imaging machine with patient in the standing position

Figure 9: Study results composite: EOS, physical tests, pain, and disability



References

1. Krapohl, B.D., *Functional evaluation of the spine in patients with breast hypertrophy.* Plast Surg Nurs, 2005. **25**(4): p. 187-9.

2. Collins, E.D., et al., *The effectiveness of surgical and nonsurgical interventions in relieving the symptoms of macromastia.* Plast Reconstr Surg, 2002. **109**(5): p. 1556-66.

3. Chiu, T.W. and C. Stone, *Stone's plastic surgery facts and figures*. 3rd ed. 2011, Cambridge: Cambridge University Press. xiii, 501 p.

4. Deyo, R.A., S.K. Mirza, and B.I. Martin, *Back pain prevalence and visit rates: estimates from U.S. national surveys, 2002.* Spine (Phila Pa 1976), 2006. **31**(23): p. 2724-7.

5. van Tulder, M.W., B.W. Koes, and L.M. Bouter, *A cost-of-illness study of back pain in The Netherlands.* Pain, 1995. **62**(2): p. 233-40.

6. Ducic, I., M.L. Iorio, and A. Al-Attar, *Chronic headaches/migraines: extending indications for breast reduction.* Plast Reconstr Surg, 2010. **125**(1): p. 44-9.

7. Freire, M., et al., *Functional capacity and postural pain outcomes after reduction mammaplasty.* Plast Reconstr Surg, 2007. **119**(4): p. 1149-56; discussion 1157-8.

8. Mosser, S.W., et al., *The anatomy of the greater occipital nerve: implications for the etiology of migraine headaches.* Plast Reconstr Surg, 2004. **113**(2): p. 693-7; discussion 698-700.

9. Brown, A.P., C. Hill, and K. Khan, *Outcome of reduction mammaplasty--a patients' perspective.* Br J Plast Surg, 2000. **53**(7): p. 584-7.

10. Chadbourne, E.B., et al., *Clinical outcomes in reduction mammaplasty: a systematic review and meta-analysis of published studies.* Mayo Clin Proc, 2001. **76**(5): p. 503-10.

11. Redaelli, A., P. Berjano, and M. Aebi, *Focal disorders of the spine with compensatory deformities: how to define them.* Eur Spine J, 2018. **27**(Suppl 1): p. 59-69.

12. Cano, S.J., et al., *The BREAST-Q: further validation in independent clinical samples.* Plast Reconstr Surg, 2012. **129**(2): p. 293-302.

13. Pusic, A.L., et al., *Validation of the breast evaluation questionnaire.* Plast Reconstr Surg, 2007. **120**(1): p. 352-3.

14. Pusic, A.L., et al., *Clinical research in breast surgery: reduction and postmastectomy reconstruction.* Clin Plast Surg, 2008. **35**(2): p. 215-26.

15. Mundy, L.R., et al., *Understanding the Health Burden of Macromastia: Normative Data for the BREAST-Q Reduction Module.* Plast Reconstr Surg, 2017. **139**(4): p. 846e-853e.

16. Cerrato, F., et al., *The impact of macromastia on adolescents: a cross-sectional study.* Pediatrics, 2012. **130**(2): p. e339-46.

17. Ouellet, J., *Personal Communication*. 2018.

18. Berberoglu, O., M. Temel, and A. Turkmen, *Effects of Reduction Mammaplasty Operations on the Spinal Column: Clinical and Radiological Response.* Aesthetic Plast Surg, 2015. **39**(4): p. 514-22.

19. Karabekmez, F.E., et al., *Does reduction mammaplasty revert skeletal disturbances in the vertebral column of patients with macromastia? A preliminary study.* Aesthetic Plast Surg, 2014. **38**(1): p. 104-12.

20. Sahin, I., et al., *Evaluation of breast reduction surgery effect on body posture and gait pattern using three-dimensional gait analysis.* Aesthetic Plast Surg, 2013. **37**(3): p. 549-53.

21. Lapid, O., et al., *The effect of breast hypertrophy on patient posture.* Arch Plast Surg, 2013. **40**(5): p. 559-63.

22. Karaaslan, O., et al., *The effect of reduction mammaplasty on the vertebral column: a radiologic study.* ScientificWorldJournal, 2013. **2013**: p. 701391.

23. Findikcioglu, K., et al., *The impact of breast reduction surgery on the vertebral column.* Ann Plast Surg, 2013. **70**(6): p. 639-42.

24. Barbosa, A.F., et al., *The impact of surgical breast reduction on the postural control of women with breast hypertrophy.* Aesthetic Plast Surg, 2013. **37**(2): p. 321-6.

25. Tenna, S., et al., *Postural variations after breast reduction: introduction of a new technique to achieve an objective analysis.* Ann Plast Surg, 2012. **68**(3): p. 261-4.

26. Foreman, K.B., et al., *The impact of breast reduction surgery on low-back compressive forces and function in individuals with macromastia.* Plast Reconstr Surg, 2009. **124**(5): p. 1393-9.

27. Benditte-Klepetko, H., et al., *Hypertrophy of the breast: a problem of beauty or health?* J Womens Health (Larchmt), 2007. **16**(7): p. 1062-9.

28. Coltman, C.E., J.R. Steele, and D.E. McGhee, *Breast volume is affected by body mass index but not age.* Ergonomics, 2017. **60**(11): p. 1576-1585.

29. Papanastasiou, C., et al., *PSRC Podium Presentation & Abstract QS 36: Quantitative Orthopaedic Spine Benefits Post Breast Reduction - Preliminary Results.* Plastic and Reconstructive Surgery, 2018. **6**(4S): p. 138.

30. Kerrigan, C.L., et al., *Reduction mammaplasty: defining medical necessity.* Med Decis Making, 2002. **22**(3): p. 208-17.

31. Kerrigan, C.L., et al., *The health burden of breast hypertrophy.* Plast Reconstr Surg, 2001. **108**(6): p. 1591-9.

32. Cabral, I.V., et al., *Increased Capacity for Work and Productivity After Breast Reduction.* Aesthet Surg J, 2017. **37**(1): p. 57-62.

33. Statcan, *Statistics Canada - Overweight and obese adults (self-reported), 2014.* 2014.

34. Gonzalez, M.A., et al., *Quality of life after breast reduction surgery: a 10-year retrospective analysis using the Breast Q questionnaire: does breast size matter?* Ann Plast Surg, 2012. **69**(4): p. 361-3.

35. Papanastasiou, C., J. Ouellet, and L. Lessard, *The Effects of Bilateral Breast Reduction on Back Pain and Spine Measurements – A Systematic Review.* Plastic and Reconstructive Surgery Global Open, 2019.

36. Papanastasiou, C., et al., *PSRC Podium Presentation & Abstract QS 29: Quantitative Spine Benefits Post Breast Reduction.* Plastic and Reconstructive Surgery - Global Open, 2019. **7**(4S): p. 121-122.

37. Pernia, L.R., et al., *Carpal tunnel syndrome in women undergoing reduction mammaplasty.* Plast Reconstr Surg, 2000. **105**(4): p. 1314-9.

38. Mick, G.J., K.L. McCormick, and H. Wakimoto, *Massive breast enlargement in an infant girl with central nervous system dysfunction.* Eur J Pediatr, 1991. **150**(3): p. 154-7.

39. Sharma, K., et al., *Unilateral gestational macromastia--a rare disorder.* Malays J Pathol, 2004. **26**(2): p. 125-8.

40. Zhong, A., et al., *Stromal-epithelial cell interactions and alteration of branching morphogenesis in macromastic mammary glands.* J Cell Mol Med, 2014. **18**(7): p. 1257-66.

41. Noczynska, A., R. Wasikowa, and T. Myczkowski, *[Hypersensitivity of estrogen receptors as a cause of gigantomasty in two girls].* Pol Merkur Lekarski, 2001. **11**(66): p. 507-9.

42. Dancey, A., et al., *Gigantomastia--a classification and review of the literature.* J Plast Reconstr Aesthet Surg, 2008. **61**(5): p. 493-502.

43. Dafydd, H., et al., *Redefining gigantomastia.* J Plast Reconstr Aesthet Surg, 2011. **64**(2): p. 160-3.

44. Gonzalez, F., et al., *Reduction mammaplasty improves symptoms of macromastia.* Plast Reconstr Surg, 1993. **91**(7): p. 1270-6.

45. Lassus, C., *A 30-year experience with vertical mammaplasty.* Plast Reconstr Surg, 1996. **97**(2): p. 373-80.

46. Matthews, J.L., et al., *Vertical Scar Breast Reduction: Does Gathering the Incision Matter?* Ann Plast Surg, 2016. **77**(1): p. 25-31.

47. Lejour, M., *Vertical mammaplasty and liposuction of the breast.* Plast Reconstr Surg, 1994. **94**(1): p. 100-14.

48. Lista, F. and J. Ahmad, *Vertical scar reduction mammaplasty: a 15-year experience including a review of 250 consecutive cases.* Plast Reconstr Surg, 2006. **117**(7): p. 2152-65; discussion 2166-9.

49. Hall-Findlay, E., *Commentary on: Vertical reduction mammaplasty utilizing the superomedial pedicle: is it really for everyone?* Aesthet Surg J, 2012. **32**(6): p. 726-8.

50. Rogliani, M., et al., *Improvement of physical and psychological symptoms after breast reduction.* J Plast Reconstr Aesthet Surg, 2009. **62**(12): p. 1647-9.

51. Romeo, M., et al., *Reduction mammaplasty and related impact on psychosexual function.* J Plast Reconstr Aesthet Surg, 2010. **63**(12): p. 2112-6.

52. Frontera, W.R. and J. Ochala, *Skeletal muscle: a brief review of structure and function.* Calcif Tissue Int, 2015. **96**(3): p. 183-95.

53. Letterman, G. and M. Schurter, *The effects of mammary hypertrophy on the skeletal system.* Ann Plast Surg, 1980. **5**(6): p. 425-31.

54. Chao, J.D., et al., *Reduction mammaplasty is a functional operation, improving quality of life in symptomatic women: a prospective, single-center breast reduction outcome study.* Plast Reconstr Surg, 2002. **110**(7): p. 1644-52; discussion 1653-4.

55. Deschenes, S., et al., *Diagnostic imaging of spinal deformities: reducing patients radiation dose with a new slot-scanning X-ray imager.* Spine (Phila Pa 1976), 2010. **35**(9): p. 989-94.

56. Dubousset, J., et al., *[A new 2D and 3D imaging approach to musculoskeletal physiology and pathology with low-dose radiation and the standing position: the EOS system].* Bull Acad Natl Med, 2005. **189**(2): p. 287-97; discussion 297-300.

57. Coriddi, M., et al., *Analysis of satisfaction and well-being following breast reduction using a validated survey instrument: the BREAST-Q.* Plast Reconstr Surg, 2013. **132**(2): p. 285-90.

58. Health, U.D.o., *Utah Health Status Survey - Interpreting the SF-12.* 2001.

59. Lab, U.o.D.-M., *Physical Therapy Clinic - 5X Sit-to-Stand Test (5XSST).*

60. Fortin, M. and M.C. Battie, *Quantitative paraspinal muscle measurements: inter-software reliability and agreement using OsiriX and ImageJ.* Phys Ther, 2012. **92**(6): p. 853-64.

61. Somoskeoy, S., et al., *Accuracy and reliability of coronal and sagittal spinal curvature data based on patient-specific three-dimensional models created by the EOS 2D/3D imaging system.* Spine J, 2012. **12**(11): p. 1052-9.

62. Kato, S., C. Debaud, and R.D. Zeller, *Three-dimensional EOS Analysis of Apical Vertebral Rotation in Adolescent Idiopathic Scoliosis.* J Pediatr Orthop, 2017. **37**(8): p. e543-e547.

63. Newton, P.O., et al., *New EOS Imaging Protocol Allows a Substantial Reduction in Radiation Exposure for Scoliosis Patients.* Spine Deform, 2016. **4**(2): p. 138-144.

64. Araujo, F., et al., *Sagittal standing posture, back pain, and quality of life among adults from the general population: a sex-specific association.* Spine (Phila Pa 1976), 2014. **39**(13): p. E782-94.

65. Joshi, S., G. Balthillaya, and Y.V.R. Neelapala, *Thoracic Posture and Mobility in Mechanical Neck Pain Population: A Review of the Literature.* Asian Spine J, 2019.

66. Nowotny, J., et al., *Body posture and syndromes of back pain.* Ortop Traumatol Rehabil, 2011. **13**(1): p. 59-71.

MASTER REFERENCE LIST

Chapter 1

1. Krapohl BD. Functional evaluation of the spine in patients with breast hypertrophy. *Plast Surg Nurs.* 2005;25(4):187-189.

2. Collins ED, Kerrigan CL, Kim M, et al. The effectiveness of surgical and nonsurgical interventions in relieving the symptoms of macromastia. *Plast Reconstr Surg.* 2002;109(5):1556-1566.

3. Chiu TW, Stone C. *Stone's plastic surgery facts and figures.* 3rd ed. Cambridge: Cambridge University Press; 2011.

4. Deyo RA, Mirza SK, Martin BI. Back pain prevalence and visit rates: estimates from U.S. national surveys, 2002. *Spine (Phila Pa 1976).* 2006;31(23):2724-2727.

5. van Tulder MW, Koes BW, Bouter LM. A cost-of-illness study of back pain in The Netherlands. *Pain.* 1995;62(2):233-240.

6. Association APT. "Move Forward" - Low Back Pain Survey. 2012.

7. Ducic I, Iorio ML, Al-Attar A. Chronic headaches/migraines: extending indications for breast reduction. *Plast Reconstr Surg.* 2010;125(1):44-49.

8. Freire M, Neto MS, Garcia EB, Quaresma MR, Ferreira LM. Functional capacity and postural pain outcomes after reduction mammaplasty. *Plast Reconstr Surg.* 2007;119(4):1149-1156; discussion 1157-1148.

9. Mosser SW, Guyuron B, Janis JE, Rohrich RJ. The anatomy of the greater occipital nerve: implications for the etiology of migraine headaches. *Plast Reconstr Surg.* 2004;113(2):693-697; discussion 698-700.

10. Brown AP, Hill C, Khan K. Outcome of reduction mammaplasty--a patients' perspective. *Br J Plast Surg.* 2000;53(7):584-587.

11. Chadbourne EB, Zhang S, Gordon MJ, et al. Clinical outcomes in reduction mammaplasty: a systematic review and meta-analysis of published studies. *Mayo Clin Proc.* 2001;76(5):503-510.

12. Redaelli A, Berjano P, Aebi M. Focal disorders of the spine with compensatory deformities: how to define them. *Eur Spine J.* 2018;27(Suppl 1):59-69.

13. Cano SJ, Klassen AF, Scott AM, Cordeiro PG, Pusic AL. The BREAST-Q: further validation in independent clinical samples. *Plast Reconstr Surg.* 2012;129(2):293-302.

14. Pusic AL, Klassen A, Cano SJ, Kerrigan CL. Validation of the breast evaluation questionnaire. *Plast Reconstr Surg.* 2007;120(1):352-353.

15. Pusic AL, McCarthy C, Cano SJ, Klassen AF, Kerrigan CL. Clinical research in breast surgery: reduction and postmastectomy reconstruction. *Clin Plast Surg.* 2008;35(2):215-226.

16. Mundy LR, Homa K, Klassen AF, Pusic AL, Kerrigan CL. Understanding the Health Burden of Macromastia: Normative Data for the BREAST-Q Reduction Module. *Plast Reconstr Surg.* 2017;139(4):846e-853e.

17. Cerrato F, Webb ML, Rosen H, et al. The impact of macromastia on adolescents: a cross-sectional study. *Pediatrics.* 2012;130(2):e339-346.

18. Ouellet J. Personal Communication. 2018.

19. Berberoglu O, Temel M, Turkmen A. Effects of Reduction Mammaplasty Operations on the Spinal Column: Clinical and Radiological Response. *Aesthetic Plast Surg.* 2015;39(4):514-522.

20. Karabekmez FE, Gokkaya A, Isik C, Saglam I, Efeoglu FB, Gorgu M. Does reduction mammaplasty revert skeletal disturbances in the vertebral column of patients with macromastia? A preliminary study. *Aesthetic Plast Surg.* 2014;38(1):104-112.

21. Sahin I, Iskender S, Ozturk S, Balaban B, Isik S. Evaluation of breast reduction surgery effect on body posture and gait pattern using three-dimensional gait analysis. *Aesthetic Plast Surg.* 2013;37(3):549-553.

22. Lapid O, de Groof EJ, Corion LU, Smeulders MJ, van der Horst CM. The effect of breast hypertrophy on patient posture. *Arch Plast Surg.* 2013;40(5):559-563.

23. Karaaslan O, Demirkiran HG, Silistreli O, et al. The effect of reduction mammaplasty on the vertebral column: a radiologic study. *ScientificWorldJournal.* 2013;2013:701391.

24. Findikcioglu K, Findikcioglu F, Bulam H, Sezgin B, Ozmen S. The impact of breast reduction surgery on the vertebral column. *Ann Plast Surg.* 2013;70(6):639-642.

25. Barbosa AF, Lavoura PH, Boffino CC, et al. The impact of surgical breast reduction on the postural control of women with breast hypertrophy. *Aesthetic Plast Surg.* 2013;37(2):321-326.

26. Tenna S, Brunetti B, Trivelli M, Salvinelli F, Persichetti P. Postural variations after breast reduction: introduction of a new technique to achieve an objective analysis. *Ann Plast Surg.* 2012;68(3):261-264.

27. Foreman KB, Dibble LE, Droge J, Carson R, Rockwell WB. The impact of breast reduction surgery on low-back compressive forces and function in individuals with macromastia. *Plast Reconstr Surg.* 2009;124(5):1393-1399.

28. Benditte-Klepetko H, Leisser V, Paternostro-Sluga T, et al. Hypertrophy of the breast: a problem of beauty or health? *J Womens Health (Larchmt).* 2007;16(7):1062-1069.

29. Coltman CE, Steele JR, McGhee DE. Breast volume is affected by body mass index but not age. *Ergonomics.* 2017;60(11):1576-1585.

30. Papanastasiou C, Fortin M, Ouellet J, Lessard L. PSRC Podium Presentation & Abstract QS 36: Quantitative Orthopaedic Spine Benefits Post Breast Reduction - Preliminary Results. *Plastic and Reconstructive Surgery.* 2018;6(4S):138.

31. Kerrigan CL, Collins ED, Kim HM, et al. Reduction mammaplasty: defining medical necessity. *Med Decis Making.* 2002;22(3):208-217.

32. Kerrigan CL, Collins ED, Striplin D, et al. The health burden of breast hypertrophy. *Plast Reconstr Surg.* 2001;108(6):1591-1599.

33. Cabral IV, Garcia ED, Sobrinho RN, et al. Increased Capacity for Work and Productivity After Breast Reduction. *Aesthet Surg J.* 2017;37(1):57-62.

34. Statcan. Statistics Canada - Overweight and obese adults (self-reported), 2014. 2014.

35. Gonzalez MA, Glickman LT, Aladegbami B, Simpson RL. Quality of life after breast reduction surgery: a 10-year retrospective analysis using the Breast Q questionnaire: does breast size matter? *Ann Plast Surg.* 2012;69(4):361-363.

Chapter 2

1. Krapohl, B.D., *Functional evaluation of the spine in patients with breast hypertrophy.* Plast Surg Nurs, 2005. **25**(4): p. 187-9.

2. Collins, E.D., et al., *The effectiveness of surgical and nonsurgical interventions in relieving the symptoms of macromastia.* Plast Reconstr Surg, 2002. **109**(5): p. 1556-66.

3. Chiu, T.W. and C. Stone, *Stone's plastic surgery facts and figures*. 3rd ed. 2011, Cambridge: Cambridge University Press. xiii, 501 p.

4. Deyo, R.A., S.K. Mirza, and B.I. Martin, *Back pain prevalence and visit rates: estimates from U.S. national surveys, 2002.* Spine (Phila Pa 1976), 2006. **31**(23): p. 2724-7.

5. van Tulder, M.W., B.W. Koes, and L.M. Bouter, *A cost-of-illness study of back pain in The Netherlands.* Pain, 1995. **62**(2): p. 233-40.

6. Ducic, I., M.L. Iorio, and A. Al-Attar, *Chronic headaches/migraines: extending indications for breast reduction.* Plast Reconstr Surg, 2010. **125**(1): p. 44-9.

7. Freire, M., et al., *Functional capacity and postural pain outcomes after reduction mammaplasty.* Plast Reconstr Surg, 2007. **119**(4): p. 1149-56; discussion 1157-8.

8. Mosser, S.W., et al., *The anatomy of the greater occipital nerve: implications for the etiology of migraine headaches.* Plast Reconstr Surg, 2004. **113**(2): p. 693-7; discussion 698-700.

9. Brown, A.P., C. Hill, and K. Khan, *Outcome of reduction mammaplasty--a patients' perspective.* Br J Plast Surg, 2000. **53**(7): p. 584-7.

10. Chadbourne, E.B., et al., *Clinical outcomes in reduction mammaplasty: a systematic review and meta-analysis of published studies.* Mayo Clin Proc, 2001. **76**(5): p. 503-10.

11. Redaelli, A., P. Berjano, and M. Aebi, *Focal disorders of the spine with compensatory deformities: how to define them.* Eur Spine J, 2018. **27**(Suppl 1): p. 59-69.

12. Cano, S.J., et al., *The BREAST-Q: further validation in independent clinical samples.* Plast Reconstr Surg, 2012. **129**(2): p. 293-302.

13. Pusic, A.L., et al., *Validation of the breast evaluation questionnaire.* Plast Reconstr Surg, 2007. **120**(1): p. 352-3.

14. Pusic, A.L., et al., *Clinical research in breast surgery: reduction and postmastectomy reconstruction.* Clin Plast Surg, 2008. **35**(2): p. 215-26.

15. Mundy, L.R., et al., *Understanding the Health Burden of Macromastia: Normative Data for the BREAST-Q Reduction Module.* Plast Reconstr Surg, 2017. **139**(4): p. 846e-853e.

16. Cerrato, F., et al., *The impact of macromastia on adolescents: a cross-sectional study.* Pediatrics, 2012. **130**(2): p. e339-46.

17. Ouellet, J., *Personal Communication*. 2018.

18. Berberoglu, O., M. Temel, and A. Turkmen, *Effects of Reduction Mammaplasty Operations on the Spinal Column: Clinical and Radiological Response.* Aesthetic Plast Surg, 2015. **39**(4): p. 514-22.

19. Karabekmez, F.E., et al., *Does reduction mammaplasty revert skeletal disturbances in the vertebral column of patients with macromastia? A preliminary study.* Aesthetic Plast Surg, 2014. **38**(1): p. 104-12.

20. Sahin, I., et al., *Evaluation of breast reduction surgery effect on body posture and gait pattern using three-dimensional gait analysis.* Aesthetic Plast Surg, 2013. **37**(3): p. 549-53.

21. Lapid, O., et al., *The effect of breast hypertrophy on patient posture.* Arch Plast Surg, 2013. **40**(5): p. 559-63.

22. Karaaslan, O., et al., *The effect of reduction mammaplasty on the vertebral column: a radiologic study.* ScientificWorldJournal, 2013. **2013**: p. 701391.

23. Findikcioglu, K., et al., *The impact of breast reduction surgery on the vertebral column.* Ann Plast Surg, 2013. **70**(6): p. 639-42.

24. Barbosa, A.F., et al., *The impact of surgical breast reduction on the postural control of women with breast hypertrophy.* Aesthetic Plast Surg, 2013. **37**(2): p. 321-6.

25. Tenna, S., et al., *Postural variations after breast reduction: introduction of a new technique to achieve an objective analysis.* Ann Plast Surg, 2012. **68**(3): p. 261-4.

26. Foreman, K.B., et al., *The impact of breast reduction surgery on low-back compressive forces and function in individuals with macromastia.* Plast Reconstr Surg, 2009. **124**(5): p. 1393-9.

27. Benditte-Klepetko, H., et al., *Hypertrophy of the breast: a problem of beauty or health?* J Womens Health (Larchmt), 2007. **16**(7): p. 1062-9.

28. Coltman, C.E., J.R. Steele, and D.E. McGhee, *Breast volume is affected by body mass index but not age.* Ergonomics, 2017. **60**(11): p. 1576-1585.

29. Papanastasiou, C., et al., *PSRC Podium Presentation & Abstract QS 36: Quantitative Orthopaedic Spine Benefits Post Breast Reduction - Preliminary Results.* Plastic and Reconstructive Surgery, 2018. **6**(4S): p. 138.

30. Kerrigan, C.L., et al., *Reduction mammaplasty: defining medical necessity.* Med Decis Making, 2002. **22**(3): p. 208-17.

31. Kerrigan, C.L., et al., *The health burden of breast hypertrophy.* Plast Reconstr Surg, 2001. **108**(6): p. 1591-9.

32. Cabral, I.V., et al., *Increased Capacity for Work and Productivity After Breast Reduction.* Aesthet Surg J, 2017. **37**(1): p. 57-62.

33. Statcan, *Statistics Canada - Overweight and obese adults (self-reported), 2014.* 2014.

34. Gonzalez, M.A., et al., *Quality of life after breast reduction surgery: a 10-year retrospective analysis using the Breast Q questionnaire: does breast size matter?* Ann Plast Surg, 2012. **69**(4): p. 361-3.

35. Papanastasiou, C., J. Ouellet, and L. Lessard, *The Effects of Bilateral Breast Reduction on Back Pain and Spine Measurements – A Systematic Review.* Plastic and Reconstructive Surgery Global Open, 2019.

36. Papanastasiou, C., et al., *PSRC Podium Presentation & Abstract QS 29: Quantitative Spine Benefits Post Breast Reduction.* Plastic and Reconstructive Surgery - Global Open, 2019. **7**(4S): p. 121-122.

37. Pernia, L.R., et al., *Carpal tunnel syndrome in women undergoing reduction mammaplasty.* Plast Reconstr Surg, 2000. **105**(4): p. 1314-9.

38. Mick, G.J., K.L. McCormick, and H. Wakimoto, *Massive breast enlargement in an infant girl with central nervous system dysfunction.* Eur J Pediatr, 1991. **150**(3): p. 154-7.

39. Sharma, K., et al., *Unilateral gestational macromastia--a rare disorder.* Malays J Pathol, 2004. **26**(2): p. 125-8.

40. Zhong, A., et al., *Stromal-epithelial cell interactions and alteration of branching morphogenesis in macromastic mammary glands.* J Cell Mol Med, 2014. **18**(7): p. 1257-66.

41. Noczynska, A., R. Wasikowa, and T. Myczkowski, *[Hypersensitivity of estrogen receptors as a cause of gigantomasty in two girls].* Pol Merkur Lekarski, 2001. **11**(66): p. 507-9.

42. Dancey, A., et al., *Gigantomastia--a classification and review of the literature.* J Plast Reconstr Aesthet Surg, 2008. **61**(5): p. 493-502.

43. Dafydd, H., et al., *Redefining gigantomastia.* J Plast Reconstr Aesthet Surg, 2011. **64**(2): p. 160-3.

44. Gonzalez, F., et al., *Reduction mammaplasty improves symptoms of macromastia.* Plast Reconstr Surg, 1993. **91**(7): p. 1270-6.

45. Lassus, C., *A 30-year experience with vertical mammaplasty.* Plast Reconstr Surg, 1996. **97**(2): p. 373-80.

46. Matthews, J.L., et al., *Vertical Scar Breast Reduction: Does Gathering the Incision Matter?* Ann Plast Surg, 2016. **77**(1): p. 25-31.

47. Lejour, M., *Vertical mammaplasty and liposuction of the breast.* Plast Reconstr Surg, 1994. **94**(1): p. 100-14.

48. Lista, F. and J. Ahmad, *Vertical scar reduction mammaplasty: a 15-year experience including a review of 250 consecutive cases.* Plast Reconstr Surg, 2006. **117**(7): p. 2152-65; discussion 2166-9.

49. Hall-Findlay, E., *Commentary on: Vertical reduction mammaplasty utilizing the superomedial pedicle: is it really for everyone?* Aesthet Surg J, 2012. **32**(6): p. 726-8.

50. Rogliani, M., et al., *Improvement of physical and psychological symptoms after breast reduction.* J Plast Reconstr Aesthet Surg, 2009. **62**(12): p. 1647-9.

51. Romeo, M., et al., *Reduction mammaplasty and related impact on psychosexual function.* J Plast Reconstr Aesthet Surg, 2010. **63**(12): p. 2112-6.

52. Frontera, W.R. and J. Ochala, *Skeletal muscle: a brief review of structure and function.* Calcif Tissue Int, 2015. **96**(3): p. 183-95.

53. Letterman, G. and M. Schurter, *The effects of mammary hypertrophy on the skeletal system.* Ann Plast Surg, 1980. **5**(6): p. 425-31.

54. Chao, J.D., et al., *Reduction mammaplasty is a functional operation, improving quality of life in symptomatic women: a prospective, single-center breast reduction outcome study.* Plast Reconstr Surg, 2002. **110**(7): p. 1644-52; discussion 1653-4.

55. Deschenes, S., et al., *Diagnostic imaging of spinal deformities: reducing patients radiation dose with a new slot-scanning X-ray imager.* Spine (Phila Pa 1976), 2010. **35**(9): p. 989-94.

56. Dubousset, J., et al., *[A new 2D and 3D imaging approach to musculoskeletal physiology and pathology with low-dose radiation and the standing position: the EOS system].* Bull Acad Natl Med, 2005. **189**(2): p. 287-97; discussion 297-300.

57. Coriddi, M., et al., *Analysis of satisfaction and well-being following breast reduction using a validated survey instrument: the BREAST-Q.* Plast Reconstr Surg, 2013. **132**(2): p. 285-90.

58. Health, U.D.o., *Utah Health Status Survey - Interpreting the SF-12.* 2001.

59. Lab, U.o.D.-M., *Physical Therapy Clinic - 5X Sit-to-Stand Test (5XSST).*

60. Fortin, M. and M.C. Battie, *Quantitative paraspinal muscle measurements: inter-software reliability and agreement using OsiriX and ImageJ.* Phys Ther, 2012. **92**(6): p. 853-64.

61. Somoskeoy, S., et al., *Accuracy and reliability of coronal and sagittal spinal curvature data based on patient-specific three-dimensional models created by the EOS 2D/3D imaging system.* Spine J, 2012. **12**(11): p. 1052-9.

62. Kato, S., C. Debaud, and R.D. Zeller, *Three-dimensional EOS Analysis of Apical Vertebral Rotation in Adolescent Idiopathic Scoliosis.* J Pediatr Orthop, 2017. **37**(8): p. e543-e547.

63. Newton, P.O., et al., *New EOS Imaging Protocol Allows a Substantial Reduction in Radiation Exposure for Scoliosis Patients.* Spine Deform, 2016. **4**(2): p. 138-144.

64. Araujo, F., et al., *Sagittal standing posture, back pain, and quality of life among adults from the general population: a sex-specific association.* Spine (Phila Pa 1976), 2014. **39**(13): p. E782-94.

65. Joshi, S., G. Balthillaya, and Y.V.R. Neelapala, *Thoracic Posture and Mobility in Mechanical Neck Pain Population: A Review of the Literature.* Asian Spine J, 2019.

66. Nowotny, J., et al., *Body posture and syndromes of back pain.* Ortop Traumatol Rehabil, 2011. **13**(1): p. 59-71.