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Understanding Breast Implant Illness, Before and After Explantation

A Patient-Reported Outcomes Study

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Background: Breast implant illness (BII) after aesthetic breast augmentation remains a poorly defined syndrome encompassing a wide spectrum of symptoms. While previously published series have observed overall symptomatic improvement after breast implant removal,^{1–3} there is a lack of studies evaluating changes in specific symptoms over time. The purpose of this study was to gain an understanding of symptoms associated with BII, and to evaluate how these symptoms change after removal of breast implants and total capsulectomy (explantation). We hypothesized that patients presenting with BII would experience both immediate and sustained improvement in constitutional symptoms after explantation. **Methods:** A retrospective study of all patients who underwent explantation by a single surgeon over 2 years was conducted. Repeated-measures analysis of variance accounting for dependency was used to compare symptoms before and after surgery. Multivariate analyses and linear regression models were used to examine the impact of patient- and implant-related factors on changes in symptoms.

Results: Seven hundred fifty patients met inclusion criteria. Mean preoperative survey score (26.19 ± 11.24) was significantly different from mean postoperative survey score at less than 30 days (9.49 ± 7.56) and greater than 30 days (9.46 ± 7.82 , $P < 0.001$). Patients with a BMI greater than 30 or those with clinically detectable contracture on examination showed greater improvement on their survey scores ($P = 0.039$, 0.034 , respectively).

Conclusions: Although BII encompasses a large range of symptoms, subjects in this study demonstrated significant and sustained improvement in 11 common symptom domains. This improvement was demonstrable within the first 30 days postoperatively and was maintained beyond 30 days. The study demonstrated a strong association of explantation and specific symptom improvement within the patient population studied. Future investigation will further elucidate possible biologic phenomena to better characterize the pathophysiology and mechanism of BII.

Key Words: breast implant illness, human adjuvant disease, breast implant, explantation

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Breast augmentation remains a popular cosmetic procedure in the United States and represented an estimated 1.2 billion dollar industry in 2016.⁴ The recent major 2019 recall of specific breast implants due to published associations with anaplastic large cell lymphoma⁵ has highlighted safety concerns with cosmetic breast implants. Although implant-related complications, such as capsular contracture,

implant rupture and malposition are well described,^{6,7} Breast implant illness (BII) remains a poorly defined and controversial complication. First described in the early 1960s as a human adjuvant disease and recently coined as BII, BII is a constellation of symptoms, unbound by a single organ system, which begins after the placement of breast implants. These symptoms may include, but are not limited to, fatigue, arthralgia, myalgia, cognitive impairment, dry eyes and mouth, alopecia, skin lesions, and Raynaud syndrome.^{1,3,8–19}

A possible pathophysiology of BII is an autoimmune or inflammatory reaction that occurs in response to a stimulating agent (silicone), and presents as a wide range of symptoms with similarities to connective tissue disease.²⁰ In the early 1980s, multiple case reports and small case series associated silicone breast implants with constitutional symptoms²¹ and coined the illness “human adjuvant disease.” The rise in these publications led to large class action lawsuits against implant manufacturers and an eventual FDA moratorium on silicone breast implants in the 1990s.²⁰ However, throughout the 1990s, multiple large-scale studies disproved an association between breast implants and connective tissue disease, resulting in liberalization of FDA restrictions. More recent reports have suggested that, for a subset of women experiencing constitutional symptoms consistent with BII, removal of the breast implants and associated capsules significantly reduces their symptoms.^{1,3,20} These studies, however, tend to group symptoms as a whole instead of examining the validity of individual symptoms.

Given the multiple reports of constitutional symptoms associated with breast implants, further investigation into individual symptoms and BII is warranted. We hypothesized that patients presenting with BII symptoms would demonstrate significant, sustained, and reproducible improvement in all tested symptom domains after explantation of the implants and total capsule removal. The aim of this study is to quantify symptoms associated with BII and study changes in these symptoms following explantation.

METHODS

A retrospective study evaluating patients requesting removal of their breast implants from 2017 to 2018 (24 months) was conducted. The study was approved by the Institutional Review Board (Case SPARTA IRB 20181267) prior to its initiation. Data collected included patient demographics, comorbidities, implant size, fill, texture, and symptoms. Inclusion criteria included all patients who presented to a single practice location requesting breast implant removal due to presumed symptoms related to the implant. Exclusion criteria included patients requesting implant exchange, implant pocket exchange, implant replacement, or patients treated with partial capsulectomy. The plastic surgery practice from which this cohort was drawn consists primarily of BII patients, referred by a variety of sources including BII support groups, former patients, rheumatologists, functional medicine providers, and naturopathic providers. Patient symptoms on all patients were quantified using a patient-reported outcome measure rating 11 common symptoms both preoperatively and at each postoperative visit. The 11 symptoms included on the survey with this exact wording were: (1) numbness and tingling in the extremities; (2) joint and/or muscle

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TABLE 1. Patient Survey and Follow-up Data

Totals	n (%)
Surveys completed (including preoperative)	750 (99.7)
Surveys completed before POD30	552 (73.6)
Surveys completed after POD30	395 (52.7)
Most recent follow-up	
Less than 30 d	258 (34.3)
30–60 d	30 (4.0)
60 d to 6 mo	220 (29.2)
6 mo to 1 y	41 (5.5)
Greater than 1 y	22 (2.9)

pain; (3) hair loss; (4) memory loss/cognitive problems; (5) dry eyes and/or blurred vision; (6) chronic fatigue; (7) breast pain; (8) rashes and/or hives; (9) food sensitivity/intolerance; (10) flu-like symptoms and/or low-grade fever; (11) difficulty breathing. Patients were asked to rate symptoms on a scale from 0 (absent) to 5 (very severe).

All patients were treated using a standardized surgical technique of total capsulectomy and implant removal further referred to as explantation in this manuscript. Capsule on the chest wall was routinely removed to the maximum extent possible; this included both anterior and posterior capsules of the implant. For patients with multiple sets of implants with capsules located in both subglandular and submuscular planes, both current and previous capsules were removed. For patients with extracapsular rupture, all silicone granuloma were removed following mapping by ultrasound examination by a radiologist experienced in detecting silicone granuloma. Partial capsulectomy was not performed on any of the study patients.

Patient demographics are reported in a descriptive, deidentified fashion to evaluate characteristics of patients who underwent removal of breast implants. Statistical analyses were performed using SAS Enterprise Guide, Version 7.1 (SAS Institute, Cary, NC). Repeated-measures analysis of variance accounting for dependency were used to compare preoperative and postoperative survey scores at less than 30 days and greater than 30 days postoperatively. Univariate and multivariate associations of various clinical, demographic and implant-related factors were assessed using linear regression models for their impact on change in survey scores. A *P* value of less than 0.05 was considered significant.

RESULTS

A total of 752 patients who underwent explantation including total capsulectomy from 2017 to 2018 were included in this analysis. Two (0.3%) subjects were excluded from the study as they did not complete any preoperative or postoperative surveys, leading to a total of 750 patients. Seven hundred fifty (99.7%) patients completed a preoperative survey, 552 (73.6%) completed a postoperative survey before postoperative day 30, and 395 (52.7%) completed a postoperative survey after postoperative day 30 (range, 30–1075 days; median, 138 days). In terms of follow-up, 258 subjects had their most recent follow-up before postoperative day 30, with 313 subjects following up after postoperative day 30. Table 1 illustrates the survey and follow-up data in greater detail.

Patients' demographic and clinical characteristics are described in Table 2. Average patient age at surgery was 45.9 years (SD = 10.8). Average age of implant at time of explantation was 12.6 years (SD = 8.6). Implant fill and texture was diverse among our cohort: 313 (41.7%) of 750 had saline implants, 413 (55.1%) had silicone implants; 555 (74.0%) had smooth implants; 150 (20.0%) had textured implants; 6 (0.8%) had polyurethane-coated implants, either smooth or textured. Four hundred sixteen (55.4%) patients had clinically

detectable contracture on examination on either side. Two hundred fifty-four (33.9%) patients had at least one self-reported preexisting illness, which is categorized mainly by organ system in Table 2.

Comparisons of symptom ratings before and after explantation are described in Table 3. There was a significant change in all 11 symptom domains rated by subjects from the preoperative period to both postoperative time periods (*P* < 0.001). There was no significant change in symptoms from less than 30 days postoperatively to greater than 30 days postoperatively, demonstrating that this improvement was sustained beyond the immediate postoperative period.

Univariate and multivariate associations of patient and implant-related factors are outlined in Table 4 and describe the impact of these factors on change in symptom scores. There was a significant

TABLE 2. Patient Demographics and Clinical Characteristics

	Total, N = 750
Age at surgery: mean ± SD, y	45.9 ± 10.8
BMI, mean ± SD	23.1 ± 4.4
BMI class, n (%)	
Normal	555 (74.0)
Overweight	141 (18.8)
Obese	53 (7.1)
Missing	1 (1.3)
Average implant size/pt weight ratio, mean ± SD	2.5 ± 0.7
Smoking status, n (%)	
Never	583 (77.7)
Current or former	165 (22.0)
Missing	2 (0.2)
Preexisting illness, n (%)	
Lyme disease	17 (2.3)
Connective tissue	3 (0.4)
Neurologic	39 (5.2)
Respiratory	23 (3.1)
Gastroenterologic	33 (4.4)
Urologic/gynecologic	31 (4.1)
Infectious	39 (5.2)
Musculoskeletal	31 (4.1)
Immunologic/allergic	16 (2.1)
Psychiatric	40 (5.3)
Malignancy	14 (1.9)
Endocrinologic	36 (4.8)
Dermatologic	17 (2.3)
Other	19 (2.5)
Age of implant, mean ± SD	12.6 ± 8.6
Material, n (%)	
Saline	313 (41.7)
Silicone	413 (55.1)
Missing	24 (3.2)
Surface, n (%)	
Smooth	555 (74.0)
Textured	150 (20.0)
Polyurethane	6 (0.8)
Missing	39 (5.2)
Location, n (%)	
Retroglandular	156 (20.8)
Retropectoral	592 (78.9)
Missing	2 (0.2)
Contracture on examination, n (%)	416 (55.4)

TABLE 3. Symptom Ratings Before and After Breast Implant Removal Surgery at <30 and >30 Days Postoperatively

	Preexplantation	<30 Days Postexplantation	≥30 Days Explantation	P
	mean ± SD	mean ± SD	mean ± SD	
Total score	26.19 ± 11.24	9.49 ± 7.56	9.46 ± 7.82	<0.0001
NT extremities	2.18 ± 1.61	0.68 ± 1.09	0.67 ± 1.12	<0.0001
Joint muscle	3.20 ± 1.50	1.07 ± 1.22	1.28 ± 1.35	<0.0001
Memory	3.11 ± 1.50	1.22 ± 1.23	1.18 ± 1.21	<0.0001
Hair	2.27 ± 1.63	1.07 ± 1.36	1.02 ± 1.25	<0.0001
Vision	2.75 ± 1.61	1.01 ± 1.80	1.04 ± 1.29	<0.0001
Fatigue	3.47 ± 1.59	1.33 ± 1.35	1.29 ± 1.39	<0.0001
Breast	2.35 ± 1.56	1.22 ± 1.13	0.65 ± 1.02	<0.0001
Rashes	1.39 ± 1.61	0.37 ± 1.18	0.40 ± 0.91	<0.0001
Food	2.58 ± 1.93	1.0 ± 1.40	1.26 ± 1.26	<0.0001
Flu	1.42 ± 1.68	0.27 ± 0.79	0.31 ± 0.82	<0.0001
Breathing	1.81 ± 1.6	0.43 ± 0.82	0.36 ± 0.91	<0.0001

correlation of body mass index (BMI) and the presence of contracture on either side with improvement in total survey score. Patients with a BMI greater than 30 (obese) demonstrated greater improvement in survey scores when compared with those with a BMI greater than 25 (normal) (17.4 vs 20.3, $P = 0.039$). Furthermore, patients with clinically detectable contracture demonstrated statistically significantly greater improvement in symptoms compared with those without contracture on examination (18.6 vs 17.3, $P = 0.028$).

DISCUSSION

The results of our study demonstrate both an immediate and sustained improvement across 11 common symptom domains following removal of breast implants and total capsulectomy in patients presenting for implant removal for presumed BII. In addition, our findings suggest that certain patient (BMI) and implant (presence of contracture) characteristics may be associated with greater symptom improvement after explantation.

Although the mechanism of BII remains unknown, multiple theories suggest an inflammatory process triggered by the introduction of silicone.^{3,21} This can be seen in a routine histologic analysis of the

capsules of one of our subjects, which reveals infiltration of inflammatory cells into the tissues surrounding the implant (Figs. 1A–B).

With this in mind, one may expect silicone implants to cause a more profound inflammatory effect compared with saline implants. However, silicone is actually present in the shells of many saline implants and can be seen as nonrefractile silicone elastomers in pathology slides.²² This may explain why removal of both saline and silicone implants leads to similar improvement in symptoms (Table 4, $P = 0.304$).

Capsular contracture is one of the most commonly identified complications of breast augmentation with some studies publishing rates of approximately 20%.²³ In our study, we noted that 55% of the patients (Table 2) had some degree of contracture. These patients experienced more significant improvement as compared with patients without contracture. Possible mechanisms include the mechanical nature of contracture that may result in significant physical symptoms including breast pain, muscle aches and pains, and difficulty breathing related to chest wall restrictive movement. Alternatively, capsular contracture can occur secondary to an inflammatory reaction⁷; thus, a particular subset of patients with capsular contracture on examination may represent a cohort with a disproportionate inflammatory response to a foreign body. The inflammatory response theory remains a plausible

TABLE 4. Univariate and Multivariate Association With Change in Survey Score After Surgery (Significant P Values Highlighted)

	Categories	P Value for Effect on the Change in Score Before and After Surgery*
Age	—	0.647
BMI class	Normal vs overweight	0.112†
	Normal vs obese	0.039†
	Overweight vs obese	0.547†
Average implant size/weight ratio	—	0.943
Smoking status	Current or former vs never	0.315
Preexisting Illness	Yes vs no	0.359
Age of Implant	—	0.866
Material	Saline vs silicone	0.304
Implant surface	Smooth vs textured	0.158
Location	RG vs RP	0.135
Contracture on either side	No vs yes	0.034
Contracture on right	No vs yes	0.069
Contracture on left	No vs yes	0.056

*Individual Mixed model analysis P value for each variable and time interaction.

†Multiple pairwise comparison using Tukey's method.

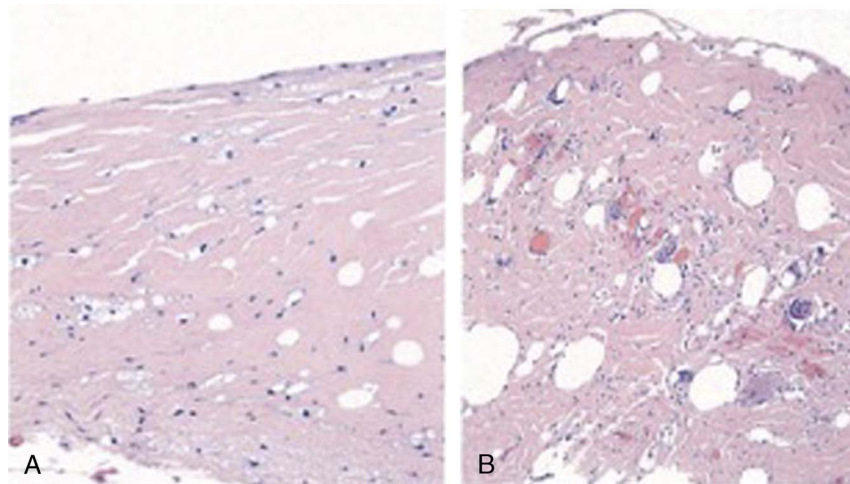


FIGURE 1. A and B, Histologic analysis of capsules surrounding an intact (A) and ruptured (B) implant. (A) Patchy mild foam cell reaction and minimal chronic inflammatory infiltrate; (B) Mild to moderate cell reaction and foreign body giant cell reaction in association with silicone. [full color online](#)

theory to support removal of the foreign body (implant) in BII patients. Similar mechanisms may be responsible for why obese patients experience greater improvement with explantation than patients with a normal BMI. As obesity is considered to be a proinflammatory state,²⁴ these patients may mount a greater inflammatory response to a trigger such as silicone.

The results of this study are subject to several limitations. The retrospective nature of the study can introduce data collection bias. For example, symptoms included on the survey reflect the most common symptoms as determined by the senior author's experience and may not represent all symptoms reported in association with breast implants. Future prospective study will include a wide range of symptoms to fully understand the nature of BII. This study is also limited by potential sampling bias, as patients requesting explantation due to the severity of their symptoms may not be representative of the overall augmented/reconstructed population. Furthermore, both preexisting conditions and symptom severity in this study are dependent on patient reports and are, thus, subject to recall bias and subjectivity; there is also no method by which to determine causality. This study also does not eliminate confounding factors such as comorbidities in its analysis. In addition, this study is limited by its quantity of long-term follow-up data, as follow-up beyond 6 months decreases significantly. This indicates the need for continued prospective study. Despite these limitations, this study quantitatively measured individual symptoms both preexplantation and at different time points postexplantation in women presenting with symptoms of BII and identified consistent improvements in symptoms after explantation in a large cohort. Efforts to balance subjectivity included a consistent ranking system for rating symptoms before and after surgery. As mentioned, an additional strength of this study is its sample size, with greater than 99% of patients completing any survey, 73.6% of patients completing a survey before 30 days postoperatively and 52.7% of patients completing a survey after 30 days postoperatively.

CONCLUSIONS

Patients presenting with symptomatic implant BII had significant immediate and sustained improvement in 11 common symptoms after removal of the implant and capsule. Future research efforts will include long-term prospective studies, as well as identification and examination of objective measures in symptomatic patients.

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