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Patient-reported systemic symptoms in women with silicone breast implants: a descriptive cohort study

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ABSTRACT

Objective An unknown portion of women with silicone breast implants (SBI) report development of systemic symptoms, recently named as 'breast implant illness (BII)'. We aim to describe the symptoms and characteristics of women with SBI reporting these systemic symptoms and compare the clinical course of women who chose to keep their implants, to women who had their implants removed.

Design Observational cohort study.

Setting Specialised BII out-patient clinic at Amsterdam UMC, the Netherlands, from 2011 to 2020.

Participants All women presenting to the BII clinic with SBI and systemic symptoms.

Results 467 women were included for baseline analyses and 398 women for follow-up. Most frequently reported systemic symptoms at baseline included fatigue (88%), arthralgia (71%), morning stiffness (59%), myalgia (48%), cognitive impairment (33%), peripheral neurological symptoms (30%) and lymphadenopathy (22%). Furthermore, 56% reported pre-existing allergies at baseline and positive antinuclear antibodies were observed in 23%. At follow-up with a median of 3.3 years (IQR 2–4), 152 women had their implants removed on clinical grounds. Symptoms improved significantly in 65 women (43%), improved moderately in 37 women (24%), did not change in 37 women (24%) and deteriorated in 13 women (9%). Women who underwent explantation showed more improvement of their systemic symptoms compared with women who did not (OR 2.9, 95% CI 1.3 to 6.2). Additionally, women who underwent explantation within 10 years after implantation improved significantly better than women who got the implants removed after 10 years (p=0.007). Lastly, local symptoms decreased from 75% to 34% after implant removal (p<0.0001).

Conclusion Most women with SBI who developed systemic symptoms experienced improvement after explantation, especially when removed within 10 years after implantation. Early recognition of the pattern of systemic symptoms in women with SBI is important and implant removal should be considered.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This observational cohort study is the first to compare a year-long clinical course of women with silicone breast implants and systemic symptoms who chose to remove their implants, to women with breast implants and systemic symptoms who chose not to have their implants removed.
⇒ The medical records from which the baseline data were extracted were not originally intended for research purposes, which may have led to under-reporting of symptoms.
⇒ All the symptoms were patient reported and thereby subjective.
⇒ Many women had startling little knowledge of their medical history regarding the implants (ie, implant brand or previous ruptured implants), which impeded us from drawing conclusions to some of our research questions.

INTRODUCTION

Silicone breast implants (SBI) have been widely used for breast augmentation and reconstruction since the 1960s, while their safety has been a subject of debate ever since. For a long time, silicone was considered an inert material, but increasing evidence undermines this assumption.[1] Multiple cohort studies observed a higher prevalence of autoimmune diseases such as Sjögren's disease, systemic sclerosis and rheumatoid arthritis in women with SBI, raising concerns about a possible association.[1–4] However, as other cohort studies and a meta-analysis found contradicting results, the evidence remains inconclusive.[5–8] Over the past decades, there have been consistent reports about women with systemic symptoms, which could not be explained by other causes, associating these symptoms with the presence of breast implants.[2 3 9] Multiple small studies report a pattern of symptoms mainly consisting of extreme fatigue, arthralgia, myalgia, morning stiffness, cognitive impairment and sicca complex, which has been termed breast implant illness (BII).[1–3 10] While the pathophysiology of this supposed association remains unclear, it has been hypothesised that these symptoms are caused by an immune response towards silicone or one of the other chemical components of the implants.[2 11] Wolfram *et al*

suggest that these symptoms are caused by a local immune response following silicone breast implantation, which, by suppressing regulatory T cells, leads to activation of immune cells such as Th1/Th17.[12] Another indication of a local immunological reaction is the recently discovered association with a rare type of T-cell lymphoma, referred to as breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), which is thought to derive from the chronic inflammation surrounding the SBI.[13–15] Contrary to earlier assumptions, these studies suggest that while SBI might be biocompatible, they are not immunologically inert.[11] In light of these considerations, a recent review article proposes that a causal link between SBI and systemic symptoms is plausible and should be accepted by the scientific community.[16]

This uncertainty and controversy are a great cause of concern among women with breast implants. A rising number of women with unexplained systemic symptoms seek advice from general practitioners or medical specialists, such as plastics surgeons, internists and rheumatologists, worrying about an association of their symptoms with their implants. At the moment, although suggestions for clinical guidelines have been proposed in the literature, no clinical guidelines with a diagnostic tract or viable treatment options are acknowledged or in use for this growing group of patients in the Netherlands.

In the Netherlands, after the Poly Implant Prothèse (PIP) implant crisis, a nation-wide specialised outpatient clinic was founded in 2011 for women with SBI who experienced unexplained systemic symptoms. Evaluation of the first 80 patients who visited this clinic resulted in a descriptive cohort study published in 2013 by Maijers *et al* who observed a significant reduction of symptoms in 69% of their patients after implant removal.[10] Interestingly, they also noticed a high prevalence of pre-existing allergies (75%).[10] Based on these results and other studies with similar findings, some of the patients with SBI who presented to the clinic with a typical pattern of symptoms were advised on clinical grounds to have their implants removed and underwent explantation.[17–19] In the last few years, the number of referrals to the clinic has been increasing rapidly, mainly due to the rising attention for this subject in the (social) media. This also underlines the importance of further clinical research, which hopefully will lead to applicable clinical advice.

Therefore, in the present observational study, we aim to describe a large cohort from this specialised clinic for women with SBI who report systemic symptoms. We observe the pattern of presented symptoms, describe the effect of implant removal on the symptoms and compare the symptoms at follow-up of women who chose to remove their implants to those who chose not to remove their implants.

METHODS

All women with breast implants and unexplained systemic symptoms who visited this specialised outpatient clinic at Amsterdam UMC, location VUmc, between 2011 and 2018 were eligible for inclusion. All types and brands of breast implants were included in this study. Patients presenting with other types of implants than breast implants, such as mesh or calf implants (n=18), were excluded.

Patient and public involvement

Patients were notified at presentation that their clinical information may be used for research purposes with the aim of improving care and developing a national care pathway for these patients, and verbal informed consent was obtained. All data were processed anonymously and patients involved will be informed of the general outcomes of the study. Importantly, the Netherlands Society of Internal Medicine, Netherlands Society of Plastic Surgeons and the patient associations were closely involved during the inception and the continuation of this out-patient clinic.

Baseline

Data were collected from medical records with the first visit serving as baseline data. During the outpatient clinic visit, an experienced consultant physician evaluated the symptoms, inquired about pre-existing allergies (including types of allergic reactions), medical history and performed a physical examination. Possible alternative explanations for the symptoms were, to the greatest possible extent, excluded using extensive blood tests and/or radiological examination. Blood tests included erythrocyte sedimentation rate, C reactive protein, haemoglobin, thrombocytes, leucocytes with differentiation, liver enzymes, renal function, thyroid stimulating hormone, vitamin D (25-OH), presence of anticyclic citrullinated peptide, rheumatoid factor, antinuclear antibodies (ANA) and other tests such as ferritin or vitamin B12 concentration on indication. The implants were assessed by physical examination and by ultrasound or MRI when imaging had not been performed prior to their visit, or on indication (eg, new asymmetry of the breasts, pain, axillary lumps etc). When the symptoms that patients presented with were compatible with BII and another explanation for their symptoms was unlikely, they were recommended to have their implants removed on their discretion.[10 20–22]

Follow-up interviews

All included patients were contacted for follow-up by a telephone interview. A full anamnesis was done, where participants were asked whether they have had their implants removed, if they currently experienced any symptoms, and how they rated their current health compared with their health at the outpatient clinic visit. Medical history, allergies and reason for implantation were verified again.

Women with breast implants at baseline were divided into two groups at follow-up: women who have had their implants removed (implant-removal group) and women who chose to keep or replace their implants (non-removal group). To assess the effect of implant removal,

Table 1 Categories for evaluation of symptoms at follow-up

Category	Criteria
Significant improvement	At least two symptoms have disappeared or all symptoms have subsided substantially
Moderate improvement	One symptom has disappeared and/or multiple symptoms are less severe
No changes	No change in symptoms
Deterioration	Extra symptoms or symptoms have worsened

the number and the severity of the reported symptoms at baseline in the implant-removal group were compared with the reported symptoms at follow-up. In order to evaluate the effect of implant removal, we used the classification as shown in table 1. Furthermore, we aimed to compare symptoms at follow-up between the implant-removal group and the non-removal group. Unfortunately, we were not always able to assess the severity of the symptoms in the non-removal group, since the symptoms were often only noted as 'present' or 'not present' in the patient records. Therefore, we chose to compare only the quantity of the symptoms between these groups using the same categorisation described in table 1. We additionally checked for possible confounders (smoking, duration of implantation, age, comorbidities of autoimmune diseases or breast cancer, implant rupture, number of implant replacements).

Statistical analysis

Obtained data were analysed using STATA Statistical Software (Statacorp, College Station, Texas, USA, V.14·1). Data are presented as a mean with SD or as absolute numbers with percentages when normally distributed. In case of non-normally distributed data, data are shown as median with IQR. The evaluation of the symptoms at follow-up in the implant-removal group and the non-removal group was analysed using multinomial logistic regression. To test for possible effect modification, the time from breast implantation to the onset of systemic symptoms was divided into early onset (<10 years) or late onset (>10 years). X^2 tests were used to compare the prevalence of symptoms at baseline between these three groups as well as between the implant-removal group and the non-removal group. The variables are presented as ORs with 95% CI. P values less than 0.05 are considered statistically significant.

RESULTS

A total of 531 women with otherwise (medically) unexplained systemic symptoms visited the clinic between 2011 and 2018, of which 467 women were included for baseline analysis (figure 1). Of these 467 women at baseline, 69 were lost to follow-up, because we were unable to reach them by phone (n=61), or because they withdrew consent (n=5), or had passed away (n=3).

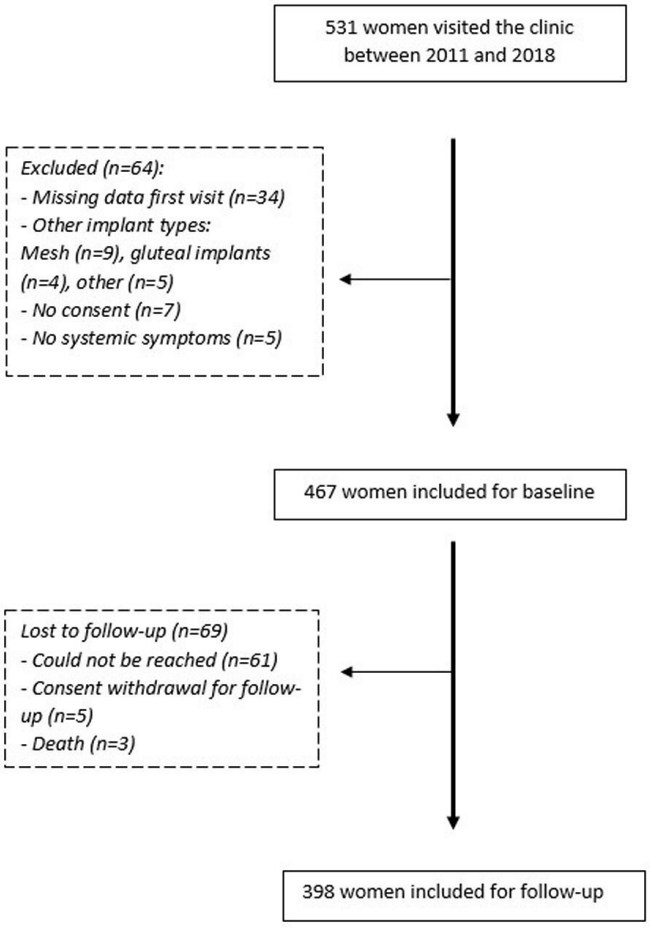

Figure 1 Study flow chart.

Baseline characteristics

The baseline characteristics are shown in table 2. Seventy-nine women (17%) already have had their implants removed before their first outpatient clinic visit, but visited the clinic either with persistent health issues or questions about probable health effects of their previous implants. Baseline characteristics did not differ between women who already underwent implant removal compared with women who still had their breast implants at presentation (data not shown).

The mean age was 48 (SD 12) years at the time of first visit. The median time between implantation and onset of symptoms was 6 (IQR 2–12) years. The majority of women received breast implants for cosmetic reasons (78%). One hundred and three women (22%) received breast implants for reconstruction following a mastectomy, after breast cancer treatment or because of a genetic predisposition for breast cancer, such as a Breast Cancer (BRCA) gene mutation. A total of 250 women (56%) reported 1 or multiple allergies, and 18 women (5%) had a radiologically proven rupture of at least 1 breast implant.

Fifty-six women reported one or more autoimmune diseases, such as rheumatoid arthritis or inflammatory

Table 2 Baseline characteristics

Total number of women	467
Implants removed before first visit	79 (17%)
Time between removal implants and clinic visit in years	1 (0–3)
Age in years	48 (±12)
History of breast cancer	71 (15%)
Intoxications	
Nicotine	
Never smoked	178 (45%)
Former smoker	101 (25%)
Current smoker	120 (30%)
Alcohol	152 (42%)
Drugs	19 (5%)
Allergies	250 (56%)
Allergic rhinitis (hay fever)	55 (12%)
Dust mite	44 (9%)
Nickel or other metals, iodine or latex	43 (9%)
Cat and dog hair	29 (6%)
Antibiotics	29 (6%)
Food allergies*	21 (5%)
Other†	85 (18%)
Reason for implantation	
Augmentation group	364 (78%)
Reconstruction group	103 (22%)
Age at implantation in years	
Augmentation group	30 (±9)
Reconstruction group	43 (±11)
Implants‡	
Total implantation time in years	12 (7–20)
Time from implantation to symptoms in years	6 (2–12)
Number of implant replacements	
None	215 (46%)
1–2	191 (41%)
3–4	45 (10%)
>4	15 (3%)

Data are presented as number (percentage), median (IQR) or mean (±SD).
*Food allergies included (among others) different kinds of fruit or nuts.
†Other allergies included allergies for wasps, laundry detergents or medication other than antibiotics.
‡No difference between the augmentation and reconstruction group.

bowel disease (online supplemental table 1). Additionally, 35 women reported thyroid disease, which were not included in the autoimmune diseases' section because many women did not know whether their thyroid disease was autoimmune mediated. Overall, 84 of the 358 women who were tested showed a positive ANA (23%), which decreased only slightly to 20% when the women who presented with a pre-existing autoimmune disease were not taken into account (online supplemental table 2). Other blood tests were mostly normal. Lastly, 35 women reported a diagnosis of fibromyalgia and two women reported a diagnosis of BIA-ALCL.

Symptoms at baseline

The reported systemic symptoms of all women are shown in table 3. The reported symptoms of the 388 women with breast implants in situ at baseline are shown separately. Most frequently reported symptoms included fatigue (88%), arthralgia (71%), morning stiffness (59%), myalgia (48%), cognitive impairment (33%), peripheral neurological symptoms (consisting mainly of tingling sensation, pins and needles, numbness, 30%) and 22% reported lymphadenopathy. Fatigue could not solely be explained by sleeping problems, since only 90 women (20%) reported sleeping problems.

Interestingly, 266 women (69%) reported local symptoms or changes of the breasts, most commonly pain (49%), changed size or shape (22%) and capsular contraction (19%) (table 3).

Symptoms at follow-up

Of the women with breast implants at baseline who were included for follow-up (n=332), 152 women (46%) reported implant removal at the time of the follow-up interview (implant-removal group), while 180 women chose to keep or replace their implants (non-removal group). There was no statistical significant difference in symptoms at baseline between these two groups. The median follow-up time between the outpatient clinic visit and telephonic interview in the implant-removal group was 3.3 years (IQR 2–4), and 3.0 years in the non-removal group (IQR 1–4.5), with a minimum follow-up time of 4 months for both groups. In the implant-removal group, the median time between removal of the implants and the interview was 2 years (IQR 1–3). The main reason for implant removal was the severity of the symptoms (71%), followed by suspected silicone leakage (25%). Additionally, 65% of the women reported one or more allergies at follow-up.

When using the classification from table 1 to evaluate the effect of implant removal on the symptoms, we observed that 65 women (43%) experienced significant improvement, 37 women (24%) experienced moderate improvement, 37 women (24%) experienced no change in symptoms and 13 women (9%) reported deterioration of their systemic symptoms after removal of their implants (table 4). Interestingly, 59% of women who removed their implants within 10 years after implantation showed significant improvement, whereas this was only 33% in the women who have had their implants for over 10 years (p=0.007). In total, 84% of the women from the implant-removal group who removed their implants within 10

Table 3 Systemic and local symptoms at baseline

	All women (n=467)		Breast implants in situ (n=388)	
Systemic symptoms	**n**	**%**	**n**	**%**
Fatigue	409	88	340	88
Arthralgia	332	71	274	71
Morning stiffness	274	59	228	59
Myalgia	226	48	180	46
Cognitive impairment*	155	33	124	32
Peripheral neurological symptoms†	142	30	117	30
Lymphadenopathy	103	22	83	22
Sleeping problems	93	20	81	21
Dermatologic symptoms	91	19	76	20
Sicca complex	78	17	61	16
Night sweats	75	16	61	16
Dyspnoea	71	15	51	13
Headaches	66	14	56	14
Flu-like feeling, fever	49	10	38	10
Recurring infections/ inflammation‡	41	9	33	9
Alopecia	30	6	23	6
Itching	22	5	21	6
Local symptoms or changes				
No local symptoms	–	–	122	31
Local symptoms	–	–	266	69
Pain	–	–	189	49
Changed size, form or consistence	–	–	87	22
Capsular contracture	–	–	73	19
Lymphadenopathy (axillary)	–	–	38	10
Changed sensibility§	–	–	19	4
Local skin disorders	–	–	14	4
Other¶	–	–	86	22

*Cognitive impairment included memory problems, word finding problems and loss of concentration.
†Peripheral neurological symptoms included feelings of numbness, pins and needles, tingling.
‡Recurring infections or inflammation included recurrent urinary tract infections, upper respiratory infections and recurring tendonitis.
§Changed sensibility included loss of sensibility, burning sensation, or hyper sensibility.
¶Other symptoms included tight feeling around the chest, recurrent infections, heavy breasts or inability to wear a bra.

Table 4 Evaluation of implant removal at follow-up (n=152)*

All women	**n**	**%**
Significant improvement	65	43
Moderate improvement	37	24
No change	37	24
Deterioration	13	9
Implants<10 years (n=56)	**n**	**%**
Significant improvement	33	59
Moderate improvement	14	25
No change	8	14
Deterioration	1	2
Implants>10 years (n=96)	**n**	**%**
Significant improvement	32	33
Moderate improvement	23	24
No change	29	30
Deterioration	12	13

*Includes all women with breast implants at baseline who had their implants removed by the time of follow-up.
%, percentage of women; n, number of women.

years experienced some degree of improvement of their symptoms.

When comparing the systemic symptoms at follow-up between the implant-removal group and the non-removal group, we found that women who removed their implants improved significantly when compared with women in the non-removal group (OR 2.9, 95% CI 1.3 to 6.2, table 5). In the implant-removal group, significantly more women experienced that one or more symptoms had completely disappeared, compared with the non-removal group (OR 2.1, 95% CI 1.3 to 3.3). This effect did not change after adjusting for possible confounding factors (data not shown).

As could be expected, local symptoms in the implant removal group decreased from 75% at baseline to 34% at follow-up (p<0.0001). In the non-removal group, local symptoms decreased from 64% at baseline to 61% at follow-up (p=0.41).

Lastly, women who already had their implants removed at baseline experienced no significant change in symptoms at follow-up (data not shown).

DISCUSSION

This study described a large clinical cohort of women with SBI who presented with systemic symptoms, which could not be explained by other causes. The most commonly reported symptoms included fatigue, arthralgia, morning stiffness, myalgia, cognitive impairment and peripheral neurological symptoms. More than half of the women presented with one or more pre-existing allergies at baseline, which tended to increase at follow-up. Additionally, two-thirds of the women who removed their implants experienced improvement of symptoms. When compared with the women who did not have their implants removed, the implant-removal group experienced significantly more improvement of their systemic symptoms at follow-up. Women who had their implants removed within 10 years after implantation showed significantly more

Table 5 Symptoms at follow-up in implant-removal group compared with the non-removal group*

	Implant-removal group (n=152)		Non-removal group (n=180)		Odds compared with having no change in symptoms, removal versus no removal		
	n	%	n	%	OR	95% CI	P value
Significant improvement	46	30	22	12	2.86	1.31 to 6.24	0.008
Moderate improvement	19	13	25	14	1.04	0.45 to 2.41	0.927
No change	19	13	26	14	–	–	–
Deterioration	68	45	107	59	0.88	0.45 to 1.71	0.712

*Note that in this Table, only the number of symptoms, and not the severity, is taken into account.
%, percentage of women; n, number of women.

improvement than women who removed their implants after more than 10 years. Presence of local symptoms had decreased by more than half in the implant-removal group, while we did not observe any change in the non-removal group.

The symptoms reported in our cohort are similar to those found in many other studies, and seem to be a good representation of the pattern of unexplained systemic symptoms in women with SBI.[19–23] Also in accordance with other studies, we found a high prevalence of local symptoms of the breasts (69%) in women with systemic symptoms, of which pain (49%) was the most common.[9 10] These local symptoms decreased significantly after implant removal, while local symptoms did not change in the group who did not remove their implants. This shows that implant removal not only has an important effect on the systemic symptoms, but on the presence of local symptoms as well.

The relatively high prevalence of positive serum ANA (23%) is interesting, but should be interpreted with caution. Prevalence of positive serum ANA is known to be higher among women and tends to increase with age. One study showed an overall prevalence of positive ANA in the US population of 13.8%, which was significantly higher in women than men (17.8% vs 9.6%).[24] Another recent study reported an overall prevalence of 15.9%, increasing up to 20.1% in older women.[25] Previous studies investigating the prevalence of positive serum ANA in women with SBI and systemic symptoms found widely varying results, ranging from 5% to 46%.[9 21 26–29] Thus, whether this observed high positive serum ANA prevalence among women with SBI and systemic symptoms is truly higher than in women without SBI or could contribute in the clinical diagnostic tract should be further investigated.

In accordance with previous studies, we found one or more pre-existing allergies in more than half of our patients (56%) at baseline.[9 10] Interestingly, at follow-up, 65% reported one or more allergies. This could be explained in multiple ways. First, it is possible that pre-existing allergies were under-reported at the first outpatient clinic visit and that the true prevalence was higher. However, it is also possible that more allergies have manifested in these patients over time. It has been suggested that silicone, or other compounds, in the breast implants may primarily cause systemic symptoms in women with a hyperimmune state or an atopic constitution.[10 30] The results of our study seem to subscribe this hypothesis, but future studies should evaluate whether this is a true risk factor for development of systemic symptoms in women with SBI.

The overall improvement of 67% in women who had their implants removed corresponds with observations from earlier studies.[9 10 17 20 26] Our present study shows that women who chose to remove their implants after developing systemic symptoms experienced significantly more improvement of their symptoms when compared with the women who chose not to remove their implants. Additionally, our results suggest that duration of implantation may be associated with chances of improvement. A possible explanation for this observation might be that the gradual gel bleed throughout the years leads to increased silicone exposure outside the implant. We should consider that this might reach a 'point of no return', where silicone particles have leaked from the implant to the extent that implant removal loses its effect. The theory that gradual gel bleed is associated with progressive symptoms, is supported by multiple studies and plays a role in several hypotheses about the disease causation.[31 32] However, further research is needed to establish whether this hypothesis could explain our findings.

In addition, it has been suggested that ruptured implants cause more severe symptoms than unruptured ones, possibly also because of increased silicone exposure.[33] Unfortunately, many of our patients did not know for sure if they had ruptured implants in the past and we did not perform MRI scans in most patients. Therefore, we only found 18 radiologically confirmed cases of implant rupture at baseline. This uncertainty about implant rupture in the past and the small number of confirmed current ruptured implants reduced our abilities to draw any reliable conclusions on this matter in our current study, but should be investigated in future studies.

It should be noted that we cannot exclude that placebo effect plays a role in the improvement after explantation, as surgery is recognised as a powerful placebo.[34] Moreover, constant (often not science based) social media reports regarding this subject can give rise to a nocebo

effect, where concerns and anxiety contribute to symptoms. Nevertheless, the observed difference in improvement from the implant removal group compared with the non-removal group after several years does warrant to take this patient group and their symptoms seriously.

This study is the first to describe a year-long clinical course of a large group of women with SBI who report systemic symptoms, for which our clinic provided us with the unique opportunity to follow-up on this patient group. Furthermore, the comparison of women with SBI and systemic symptoms who chose to remove their implants, to women who did not remove their implants, had not been described before. By classifying the effect of implant removal with different degrees of improvement, we evaluated this effect as objectively as possible and aim to offer clinicians and patients more insight regarding expectations after surgery.

Lastly, the importance of early recognition is emphasised by the evaluation of the group of women who already had their implants removed at baseline. At follow-up, their symptoms had not changed or, in a few cases, even deteriorated. At the moment, no treatment options for this group are available, besides supportive care such as rehabilitation or physical therapy. This lack of available treatment options when implant removal has had no effect, underlines the necessity of early recognition and consideration of implant removal in women who develop systemic symptoms.

Unfortunately, we noticed that many women had startling little knowledge of their medical history regarding the implants, that is, the brand and/or type, or whether earlier (explanted) implants ever had ruptured. The poor documentation and quick turnover of many private clinics often made it impossible to recover this information. For this reason, the Dutch Breast Implant Registry (DBIR) was founded in 2015 as an initiative of the Dutch Society of Plastic Surgery, which aims to register and monitor the quality of care and implants.[35] For now, we intentionally chose to include women with all brands and types of breast implants and all reported systemic symptoms for a broader overview. Hopefully, for future studies, the DBIR will be the foundation for more detailed registration and documentation.

This study has some important limitations. First, because of our observational, single-centre study design with patient-reported symptoms, we cannot exclude an effect from reporting bias, selection bias or recall bias. We should consider that women who visited our clinic had read up about BII and its typical symptoms, and therefore could have reported more of these symptoms. Furthermore, it is possible that women with systemic symptoms and ruptured implants had them removed instead of getting a referral to our clinic, leading to selection bias (underestimation of implant ruptures in our population). Second, our baseline data were collected from medical records, which were not originally intended for research. Therefore, under-reporting of symptoms at baseline may have led to a relative overestimation of symptoms at follow-up, where a more elaborate anamnesis with regard to typical symptoms was performed. However, we still found a significant reduction in symptoms after implant removal at follow-up, which could indicate that the true symptom improvement might be even greater. Third, many reported symptoms are also very common in the general population (ie, fatigue). We cannot exclude that some symptoms had multiple or other causes, even though alternative explanations were extensively examined and excluded. Last, the decision to remove the implants was physician and patient driven, so no randomisation took place. Therefore, it is possible that the group who chose implant removal differs from the group who chose not to have their implants removed. We did not find any significant differences between these groups at baseline in regard to their baseline characteristics or reported symptoms, except for a small difference in reported local symptoms between these groups (74% in the implant-removal group vs 64% in the non-removal group).

In conclusion, we believe applicable clinical advice can be extracted from this observational study. Our results show that implant removal in women with breast implants who develop systemic symptoms reduces the symptoms in most of these women, which differs significantly from women who chose not to remove their implants. Furthermore, local symptoms decrease by more than half after implant removal. Importantly, the reduction in systemic symptoms is significantly higher in women who removed their implants within 10 years after implantation. Therefore, early recognition of these symptoms is important and implant removal should be considered in women with SBI who develop this pattern of systemic symptoms.

Contributors KAS: literature search, study design, data collection, data analysis, data interpretation, writing and final approval of the manuscript. MS: literature search, data collection, data analysis, data interpretation, writing and final approval of the manuscript. CJMdB: study design, data collection, data interpretation and final approval of the manuscript. FBN: data interpretation and final approval of the manuscript. YB: data collection, data interpretation and final approval of the manuscript. PWN: study design, data interpretation and final approval of the manuscript. PWN acts as guarantor for the final manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants. This study was reviewed by the Ethical Review Board of the Amsterdam UMC, VU University Medical Center Amsterdam (reference number: 2021.0200). It was determined that the Medical Research Involving Human Subjects Act (WMO) does not apply to this study, and necessity for written informed consent was waived. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The data that support the findings of this study are available from the corresponding authorupon a reasonable request and when allowed by local privacy regulations.

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