JPRAS Open 40 (2024) 85–94

Contents lists available at ScienceDirect

JPRAS Open

journal homepage: www.elsevier.com/locate/jpra

Review Article

Unveiling the Enigma: Exploring capsular contracture–Unraveling its link with autoimmune disorders and comprehensive examination of predisposing factors

Bikona Ghosh[a,*], Alsalt AL-Busaidi[b], Mehul Sinha[c], Yeisson Rivero-Moreno[d], Jose Carlos Del Castillo Miranda[e], Darren Gopaul[f], Sarosh Sarwar[g]

[a] Dhaka Medical College & Hospital, Dhaka, Bangladesh
[b] Royal College of Surgeons in Ireland (RCSI), Dublin, Ireland
[c] Kasturba Medical College, Mangalore, India
[d] Universidad de Oriente, Venezuela
[e] Universidad Peruana Cayetano Heredia, Lima, Peru
[f] University of the West Indies, Trinidad and Tobago
[g] Fazaia Medical College, Air University Islamabad, Pakistan

ARTICLE INFO

Article history:
Received 24 October 2023
Accepted 28 January 2024
Available online 2 February 2024

Keywords:
Breast augmentation
Breast implant
Capsular contracture
Risk factors
Breast surgery

ABSTRACT

Introduction: Breast augmentation, a popular cosmetic surgery using devices like silicone implants, can lead to a common issue called capsular contracture (CC). This condition involves the formation of fibrous tissue around the implants and can be influenced by variables like immunological and bacterial factors. This study aimed to explore the impact of autoimmune diseases (ADs) on CC along with other factors influencing future clinical decisions.
Methods: A systematic review of electronic databases was conducted using PubMed, Web of Science, Scopus, EMBASE, and involving adult patients (>18) with CC and ADs after breast surgery using MeSH terminology using a broad search strategy. All searches were performed and analyzed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, and duplicates were removed with Rayyan. Two independent investi-

* Corresponding author at: Dhaka Medical College and Hospital, Dhaka, Bangladesh.
E-mail address: bghosh6@jh.edu (B. Ghosh).

https://doi.org/10.1016/j.jpra.2024.01.015

gators extracted and assessed the data involving demographics and baseline data related to CC and AD.

Results: The incidence of CC varied (2.3%-4.1%). Subglandular placement and older device age raised risk. SERI Surgical Scaffold complications included necrosis, seroma, hematoma, implant loss, and infection; CC was associated with necrosis. Natrelle 410 implants showed lower 10-year CC risk than round gel implants. Acellular dermal matrix implant-based breast reconstruction with radiotherapy (RT) correlated with 20.7% post-RT CC. Previous research demonstrated no significant connection between silicone gel implants and ADs. Biofilm, surgical site infection, implant features, and interventions emerged as frequent CC risk factors.

Conclusion: Finding appropriate techniques to reduce the risk factors associated with CC together with providing comprehensive patient counseling on these factors will definitely improve the patient-centered outcome of breast implant surgery.

Introduction

Breast augmentation is one of the most common cosmetic surgeries in the United States. Breast implants are considered medical devices used to modify the shape and size of women's breasts and construct new breasts after removal of the breast (mastectomy), for aesthetic purposes (mammoplasty), and more. Breast implants have been made from various materials, including sponges, silicone, and saline, and each implant type has advantages and disadvantages.[1]

Silicone breast implants are the most widely used and recognized substance for breast augmentation.[2] They have been used for over five decades in cosmetic and reconstructive breast surgeries. Over a million women have received silicone breast implants worldwide, excluding unregistered implantations, which might raise this figure considerably.[3] There are two common forms of silicone breast implants: a silicone outer shell with a silicone gel filling or a silicone outer shell with a different filling, such as saline.[2] Compared to saline breast implants, the prevailing belief is that the post-surgical mechanical behavior of silicone breast implants is more similar to normal breast tissue.[4]

The most common complication after breast augmentation surgery is capsular contracture (CC) of breast implants, with a reported prevalence of 5–19% refers to breast augmentation surgery and 19–25% refers to breast reconstructions.[5] CC is a local problem caused by an overly fibrotic foreign body reaction to the implant.[2] There is no apparent reason why CC of breast implants occurs.[5] It is hypothesized to be a chronic inflammatory reaction by innate immune cells, leading to fibrosis from collagen synthesis that causes pain and excessive firmness.[2,3]

Physiologically, almost all patients develop a capsule surrounding the breast implants as part of the body's normal reaction to foreign materials. However, some patients may develop an abnormally thick fibrous capsule associated with pain, contracture, and distortion of the breast.[5] Other risk factors, such as immunological and bacterial factors, play a significant role in developing CC.

The Baker classification system is used to classify CC based on the patient's clinical findings. This system has four classes; class I defines a breast that looks and feels completely natural. In contrast, class II describes a breast with minor contracture in which the surgeon can discern that surgery was performed, but the patient is asymptomatic. Classes I and II are not clinically significant. Classes III and IV are clinically significant and symptomatic, with class III indicating mild contracture with some hardness felt by the patient, and class IV describes a severe, visible contracture with symptoms.[6]

Table 1
Detailed search strategy for PubMed, SCOPUS, and Web of Science.

Database	Search string	Records identified (*n*)	Filters
PubMed	((autoimmune disease) OR (capsular contracture)) AND (breast implant or tissue expander)	222	2013–2023
Scopus	(ALL (autoimmune AND disease) AND ALL (capsular AND contraction) OR ALL (capsular AND contracture) AND ALL (breast AND implant) OR ALL (tissue AND expander)) AND PUBYEAR > 2012 AND PUBYEAR < 2024	105	2013–2023
Web of science	autoimmune diseases (All Fields) and capsular contracture (All Fields) and breast implant (All Fields)	25	–
EMBASE	(('implant capsular contracture'/exp OR 'implant capsular contracture') AND breast AND implant OR (tissue AND expander)) AND autoimmune AND disease	15	–

Some relations between breast implants and autoimmune diseases (ADs) have been described. For example, the autoimmune/inflammatory syndrome induced by adjuvants (ASIA), also known as Shoenfeld's syndrome, encompasses several autoimmune conditions/phenomena triggered by exposure to materials with adjuvant activity known to augment an antigen-driven immune response. In some inherently vulnerable patients, they act as second hits to trigger or unmask an AD, which ranges from generalized non-specific constitutional symptoms and autoantibody production to a new onset of a fully-fledged autoimmune syndrome.[7]

Currently, little is known about the opposite relationship: how ADs influence the function of breast implants. ADs are relatively common comorbidities in the female population. For example, in North America, systemic lupus erythematosus prevalence ranges from 48 to 366.6 per 100,000 individuals.[8] Therefore, it is expected that ADs are most likely present in individuals with breast implants. Still, their exact effect on complications such as CC has yet to be studied.

Hence, our systematic review aimed to evaluate the correlation between ADs and the probability of developing CC following breast implant surgery and present an in-depth review of the associated risk factors.

Methodology

Research aim and search strategy

This systematic review were performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines as shown in the flow diagram in Figure 1. The study was registered on PROSPERO as CRD42022373188. The literature search was carried out according to a predetermined protocol, and the following criteria were used to screen the studies-

- P (Population): Adult (>18 years) who have had breast implantation
- I (Intervention): Breast implantation surgery
- C (Comparison): Included population who did not have CC
- (Outcomes): Included population who had CC

Search equations were carefully designed including relevant MeSH terms, and thorough searches were performed on 4 different databases – PubMed, SCOPUS, EMBASE, and World of Science (Table 1). Articles from the search results were uploaded to Rayyan, and a thorough search for duplicates was performed. All the articles >80% similar to other articles were deleted after careful data evaluation.

Selection criteria

After detailed discussion among the authors, inclusion and exclusion criteria were established for data extraction (Table 2). Included were Studies focused on patients >18 years of age, Original Studies, Observational Studies, and Systematic Reviews and Meta-Analyses relevant to the research question.

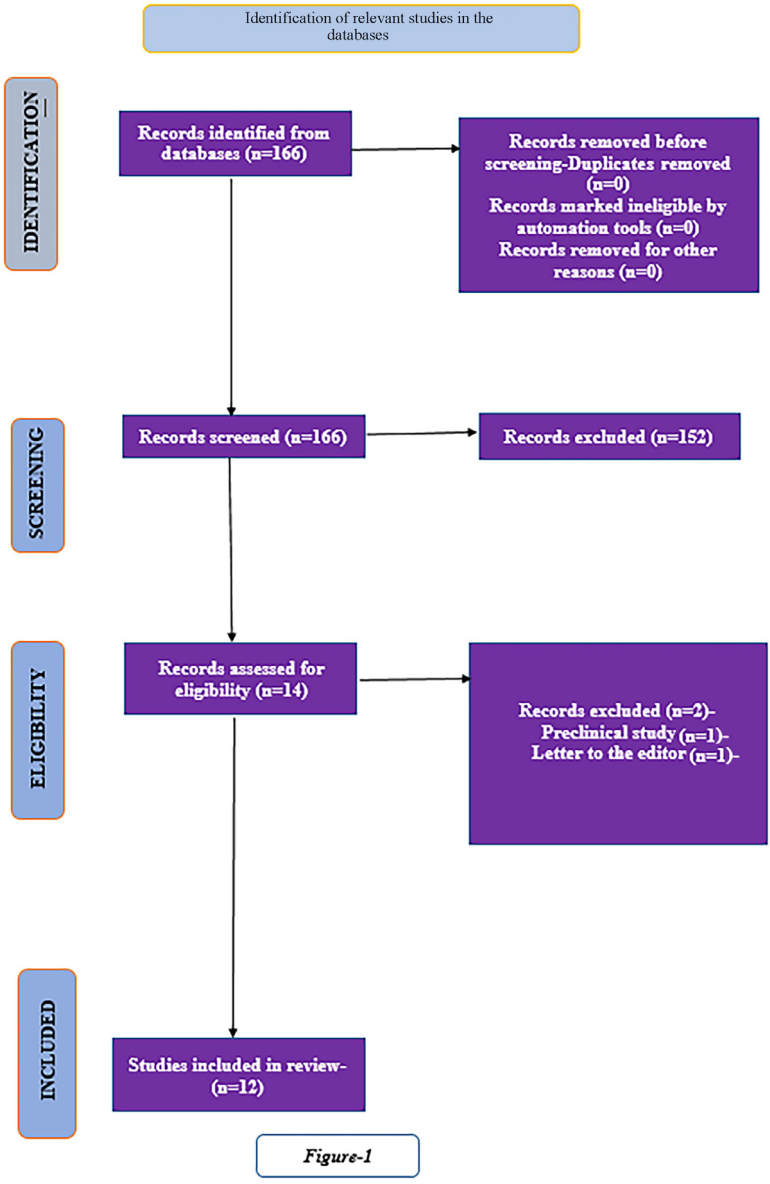

Figure 1. Schematic diagram of study selection (PRISMA).

Editorials, commentaries, and short communications were excluded. Articles that were not published in English and those not relevant to the research question were also excluded.

Data extraction and management

A standard template based on the Cochrane Consumers and Communication Review group's extraction template was followed for extraction of data from the articles for quality assessment and evidence synthesis. The information extracted included- authors, database, journal, date of publica-

Table 2
Inclusion and exclusion criteria for study selection.

	Inclusion	Exclusion
Population	Adults (>18 years) who have had breast implantation	A. Animal studies B. Studies not published in English C. Not relevant to the study E. Low screening score F. Non-blinded study
Intervention	Breast Implant Surgery	
Comparators	Included population who did not have capsular contraction	
Study designs	Original Studies, Observational Studies, Systematic Reviews and Meta-Analysis, Case series	Editorials, short communications, commentaries

tion, type of article, DOI, original title, full article abstract, applied methodology, and results. Retrieved records were screened for abstract, title, or both, and the full text of potentially relevant articles were investigated and classified as included or excluded studies. Four authors extracted the relevant data, and any discrepancies were discussed and resolved as needed.

Analysis and synthesis of the data

The findings of the included studies were integrated and presented in a cohesive and narrative manner. Data regarding the type and duration of the implant were gathered to examine the occurrence of CC. Furthermore, a comparison was made among the studies in terms of the severity of CC and ADs. This review enabled us to recognize the frequently observed symptoms, risk factors, preferred imaging techniques, and complications associated with the condition.

Quality assessment

For case reports and case series, the CARE guidelines (for CAse REports) tool was used. Other observational studies, such as case-control, cohort, or cross-sectional studies, were assessed using Strengthening the Reporting of Observational Studies for Epidemiology (STROBE) guidelines. The PRISMA checklist was used to evaluate the studies, whereas JADAD guidelines were used for randomized controlled trials. Finally, ethical and bias criteria were assessed for all studies to provide relevant information to answer the research question.

Evaluation of the studies

The selection of studies was performed using abstract screening and then reading the entirety of selected papers. Data such as basic demographics, presenting symptoms, incidence of CC, common risk factors, and complications were recorded using Microsoft Office Excel. Assessment of quality was performed using a checklist corresponding to the appropriate study type. Articles with a score greater than 70% were included for further analysis.

Results

The incidence of CC ranged from 2.3 to 4.1 percent. A study conducted by McGuire P *et al* showed that subglandular placement was the strongest risk factor for the development of CC (adjusted risk ratio [aRR]: 2.89; $P < .0001$). Other risk factors included older device age, periareolar incision site (both $P < .0001$), higher body mass index levels (aRR: 1.03; $P = .0026$), and absence of povidone-iodine pocket irrigation (aRR: 2.00; $P = .0006$).[9]

In a prospective cohort study, complications from using SERI Surgical Scaffold included tissue necrosis, seroma, hematoma, implant loss, CC, and breast infection. The only instance of CC was in a patient with tissue necrosis requiring debridement and secondary closure.[10]

At ten years, the risk of CC with the Natrelle 410 implant was lower than that reported with standard round gel implants.[11] In a prospective cohort of 2795 patients who received Natrelle 410 implants, analyzed at two years, complication rates were low, with CC occurring in 3.3%; 31 patients experiencing CC had the implant removed.[11]

An observational study including 467 women with silicone breast implants (SBIs) analyzed at baseline and 398 women at follow-up found that 19% of women complained of CC.[12]

In a study from Maartje et al, two groups of patients with complaints due to silicone-containing breast implants were compared. A cohort of 100 patients was analyzed for silicone breast implant-related complaints in 2014 in the Netherlands ('Maastricht cohort').[13] A cohort of 100 patients diagnosed at Baylor College of Medicine, Houston, Texas, USA with 'Adjuvant Breast disease' due to SBIs or silicone fluid injections between 1985 and 1992 was described in 1994 by Shoaib et al[14]

In the Maastricht cohort, local problems were frequently observed: CC ($n = 29$), sweating and/or leakage of the silicone implant ($n = 13$), implant rupture ($n = 25$), dislocation of the implant ($n = 3$), and local tenderness ($n = 4$). Furthermore, 70 patients had painful lymphadenopathy involving the axillary regions, often with cervical and/or inguinal lymphadenopathy.[13] In the Baylor College of Medicine 1994 cohort, 76 patients suffered from local problems defined as CC, tenderness, soreness or pain of the breasts, burning and swollen breasts, infections, numbness of the nipples, or discharge from the nipples. Fifty-eight patients had lymphadenopathy.[14]

A study from Anuradha et al that evaluated outcomes and complications in patients with single-stage acellular dermal matrix implant-based immediate breast reconstruction with and without radiotherapy (RT) showed that 20.7% had post-RT CCs. In the non-RT group, 7.25% had CCs.[15]

A retrospective cohort study by Edworthy et al recruited 1576 female participants who underwent breast implantation from 1978 to 1986, including 1112 who received silicone gel-filled implants. The study results did not support the theory that silicone gel-filled implants promote connective tissue diseases (CTDs).[16] Similarly, an observational study and a systematic review performed by Kjøller et al and Balk et al in 2001 and 2016, respectively, found no association between silicone gel-filled implants and CTDs.[17,18]

Similar results were obtained in a systematic review by Englert et al in 2005 showing that there was no correlation between exposure to augmentation mammoplasty and symptoms of different CTDs.[19] However, the exposed cohort had a higher incidence of axillary adenopathy and low titer antinuclear antibody detection. Breast CC and postoperative digital vasospasm were more prevalent in women with axillary adenopathy.

A systematic review performed in 2020 by Enkhmaa et al showed that biofilm, surgical site infections (SSIs), past CC, or fibrosis history, radiation therapy history, and implant features were also frequent risk factors for CC. Acellular dermal matrix, leukotriene (LTE) inhibitors, surgical procedures, antibiotic prophylaxis or irrigation, and other interventions all helped to lower the incidence of CC.[20]

Discussion

CC is the leading complication after breast augmentation or reconstruction with breast implants.[21] The pathogenesis of CC is likely multifactorial, with the innate and adaptive immune systems playing a significant role.[21] The silicone in breast implants activates monocytes and macrophages, and lymphocytes are the predominant immune cells within the capsule.[22]

The findings in this review are consistent with previous studies and indicate that risk factors for CC are multifactorial, with demographic and implant characteristics consistently playing a vital role in the pathogenesis. Although CC remains the most common complication following breast implant surgery, the exact etiology remains to be elucidated.[23]

Women with breast implants have an increased risk of autoimmune and/or rheumatic conditions compared to implant-free women.[24] Symptoms of Sjogren's syndrome, such as dry eyes, dry mouth, dry skin, and difficulty swallowing, are more prevalent among women with breast implants. Rheumatoid arthritis is also more likely to be found in women with breast implants.[25,26]

Breast implants have also been correlated with scleroderma.[27] Silicone can migrate from the implant to the body and induce a chronic inflammatory process.[28] Silicone-related autoimmune adverse

events termed 'silicosis' often include fatigue, cognitive impairment, arthralgia, myalgia, fever, dry eyes, and dry mouth.[29]

Approximately 2–2.5% of patients undergoing one of the most common surgeries in the United States, i.e., breast augmentation and reconstruction, experience SSIs. Although breast augmentation is considered an aseptic procedure, bacterial contamination from tissues is a potential source of infection. Various factors can contribute to an elevated risk of SSIs, including weight, poor nutrition, obesity, diabetes mellitus, smoking, immunodeficiency, and extended hospital stays. The significance of infection in the etiopathogenesis of CC is not entirely understood, although some studies hypothesize that biofilm from coagulase-negative Staphylococci has an essential detrimental effect.[30] Several studies have discovered links between the presence of bacteria and CC.[31] This notion is reinforced further by studies that suggest that prophylactic or postoperative antibiotic administration appears to minimize the incidence of CC but with inconsistent results.[32] Many studies have also examined the role of local antibiotics and/or irrigation in preventing CC. The use of local antibiotics in concert with irrigation has been shown to reduce CC.[33] De Kerckhove et al. described a detailed correlation and pathogenesis of biofilm as a significant factor involved in CC. Biofilm exists in attached forms to tissues or solid forms/implants.[30] It significantly induces chronic inflammation in the host's body by evading and manipulating the host's immune system. Bacterial biofilms are responsible for increased expression of growth factors, e.g., TGF-b, which cause excessive fibrosis for prolonged periods, causing scarring, thus inducing CC. They are usually part of the host's skin, gut, and internal areas of the breast. The most commonly identified organisms are *Staphylococcus epidermidis* and *Propionibacterium acnes*.[30]

CC is traditionally treated surgically, although it is crucial to emphasize that treatment is only suggested in grades III and IV CC. A total capsulectomy with site change has been reported to be the most prevalent corrective surgical procedure. Capsulectomy with or without a capsulotomy has been described as the 'gold standard' treatment. Although capsulotomy is an effective surgical treatment for CC, CC tends to recur; thus, repeated treatments may be required to maintain soft breasts.[34,35] Surgical intervention can increase the risk of CC recurrence by approximately 25% during the first year.[36]

A more recent surgical treatment procedure has been developed that entails the development of a neo-pectoral pocket in which the implant is placed. In order to avoid further tissue damage, a new sub-pectoral plane is created that extends deep into the pectoralis major muscle but is superficial to the anterior capsule; this permits the existing capsule to be used and gives a new vascularized pocket in which to insert a new textured implant. It is typically performed through an inframammary incision.[37] A retrospective study of 198 patients, of whom 69.7% had CC and were treated with revisionary breast surgery with the creation of a neo-pectoral pocket, showed a significant success rate in contracture reduction.[38]

A spectrum of pharmacological and non-pharmacological strategies has been investigated to prevent CC in breast implantation.[33] Initially, polyurethane-coated implants were used, though their discontinuation was immediate. The proof of genotoxicity followed. Implementation of both absorbable and non-absorbable mesh materials has shown efficacy in diminishing the prevalence of infection and necrosis.[33] Furthermore, applying zwitterionic polymers has exhibited the potential to attenuate broader immune and inflammatory reactions. From a surgical perspective, adopting the sub-pectoral approach instead of areolar/peri–areolar and inframammary techniques has markedly decreased CC.[33] In parallel, perioperative administration of antibiotics, including second-generation cephalosporin, gentamicin, and vancomycin, has been implemented as an effective prophylactic measure in many cases to prevent SSIs and CC.[33] The irrigation of implants and implant pockets with sterile solutions, complemented by administration of triple antibiotic formulations, is also a popular technique. Moreover, topical administration of antibiotics has also shown promising results for reducing CC risk, thus enhancing overall outcomes of implant-based procedures.[33]

This study presents a comprehensive analysis of the multifaceted factors influencing CC after breast implant surgery, with a specific focus on the role of ADs in this complication. By conducting a systematic review of the current literature, this study elucidates the intricate relationship between ADs and CC, shedding light on the nuanced interplay of immunological factors in the development of fibrous tissue around implants. Notably, this research highlights the diverse array of contributing factors, from

implant placement techniques to device characteristics and patient-related variables, providing clinicians with a holistic understanding of CC risk factors. Importantly, it synthesizes current evidence, underlining the absence of a significant direct link between silicone gel implants and ADs while emphasizing the prominence of biofilm, SSIs, and implant-specific features as contributors to CC. This comprehensive analysis serves as a valuable resource for clinicians, offering insights crucial to enhancing patient counseling, refining surgical approaches, and ultimately improving the overall outcomes of breast augmentation surgeries.

Limitation and conclusion

Although a thorough methodology was followed and executed meticulously, this study is not free from limitations. First, the data extracted from the included study only represents the viewpoint of the respondents. The non-respondents' perspectives could add more significant findings regarding this topic. Future studies should focus on prospectively following the surgical patients over time to observe the complication rates among patients with autoimmune disease vs those without. Second, the timeline only captured the latest scenario in the field and could have missed some past data on this topic. Third, articles that were not in English could have provided more insight in evaluating the said association with CC. Finally, this study is not free from recall bias from the respondents, as patients suffering from these complications tend to report and respond more than the ones without complications.

CC is one of the most common surgical complications after breast implant and requires more research into the impactful variables and risk factors. The most common risk factors included autoimmune disease; SSIs, considering the roles of bacteria and biofilm, for which postoperative antibiotics reduced the complication rate; newer surgical techniques such as creating neo-pectoral pockets for implant placement; and using areolar and sub-pectoral approaches. Moreover, topical administration of antibiotics showed promising data to reduce CC.

Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

Ethical approval

Not required.

Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

Declaration of competing interest

The authors declare there is no conflict of interests.

CRediT authorship contribution statement

Bikona Ghosh: Conceptualization, Data curation, Formal analysis, Methodology, Writing – original draft, Writing – review & editing, Supervision, Validation, Project administration, Visualization. **Alsalt AL-Busaidi:** Writing – original draft, Writing – review & editing. **Mehul Sinha:** Writing – original draft. **Yeisson Rivero-Moreno:** Writing – original draft. **Jose Carlos Del Castillo Miranda:** Writing – original draft. **Darren Gopaul:** Writing – original draft. **Sarosh Sarwar:** Writing – original draft.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi: 10.1016/j.jpra.2024.01.015.

References

1. Johnson M. Breast implants: History, safety, and imaging. *Radiol Technol*. 2013;84(5):439M–515M quiz 6M-20M.
2. Siggelkow W, Faridi A, Spiritus K, Klinge U, Rath W, Klosterhalfen B. Histological analysis of silicone breast implant capsules and correlation with capsular contracture. *Biomaterials*. 2003;24(6):1101–1109.
3. Dolores W, Christian R, Harald N, Hildegunde P, Georg W. Cellular and molecular composition of fibrous capsules formed around silicone breast implants with special focus on local immune reactions. *J Autoimmun*. 2004;23(1):81–91.
4. Daniels AU. Silicone breast implant materials. *Swiss Med Wkly*. 2012;142:w13614.
5. Bachour Y. Capsular Contracture in breast implant surgery: Where are we now and where are we going? *Aesthetic Plast Surg*. 2021;45(3):1328–1337.
6. Spear SL, Baker Jr JL. Classification of capsular contracture after prosthetic breast reconstruction. *Plast Reconstr Surg*. 1995;96(5):1119–1123 discussion 24.
7. Mir TH, Khan AK, Parvaiz MO, Rath PD, Sharma A. ASIA syndrome with severe lupus - A case report. *Lupus*. 2022;31(12):1532–1535.
8. Barber MRW, Drenkard C, Falasinnu T, et al. Global epidemiology of systemic lupus erythematosus. *Nat Rev Rheumatol*. 2021;17(9):515–532.
9. McGuire P, Reisman NR, Murphy DK. Risk factor analysis for capsular contracture, malposition, and late seroma in subjects receiving natrelle 410 form-stable silicone breast implants. *Plast Reconstr Surg*. 2017;139(1):1–9.
10. Fine NA, Lehfeldt M, Gross JE, et al. SERI surgical scaffold, prospective clinical trial of a silk-derived biological scaffold in two-stage breast reconstruction: 1-year data. *Plast Reconstr Surg*. 2015;135(2):339–351.
11. Cordeiro PG, McGuire P, Murphy DK. Natrelle 410 extra-full projection silicone breast implants: 2-year results from two prospective studies. *Plast Reconstr Surg*. 2015;136(4):638–646.
12. Spit KA, Scharff M, de Blok CJ, Niessen FB, Bachour Y, Nanayakkara PW. Patient-reported systemic symptoms in women with silicone breast implants: A descriptive cohort study. *BMJ Open*. 2022;12(6):e057159.
13. Colaris MJL, de Boer M, van der Hulst RR, Cohen Tervaert JW. Two hundreds cases of ASIA syndrome following silicone implants: A comparative study of 30 years and a review of current literature. *Immunol Res*. 2017;65(1):120–128.
14. Shoaib BO, Patten BM, Calkins DS. Adjuvant breast disease: An evaluation of 100 symptomatic women with breast implants or silicone fluid injections. *Keio J Med*. 1994;43(2):79–87.
15. Apte A, Walsh M, Balaji P, Khor B, Chandrasekharan S, Chakravorty A. Single stage immediate breast reconstruction with acellular dermal matrix and implant: Defining the risks and outcomes of post-mastectomy radiotherapy. *Surgeon*. 2020;18(4):202–207.
16. Edworthy SM, Martin L, Barr SG, Birdsell DC, Brant RF, Fritzler MJ. A clinical study of the relationship between silicone breast implants and connective tissue disease. *J Rheumatol*. 1998;25(2):254–260.
17. Kjøller K, Friis S, Mellemkjær L, et al. Connective tissue disease and other rheumatic conditions following cosmetic breast implantation in denmark. *Arch Intern Med*. 2001;161(7):973–979.
18. Balk EM, Earley A, Avendano ES, Raman G. Long-term health outcomes in women with silicone gel breast implants. *Ann Intern Med*. 2016;164(3):164–175.
19. Englert H, Joyner E, Mcgill N, et al. Women's health after plastic surgery. *Intern Med J*. 2001;31(2):77–89.
20. Luvsannyam E, Patel D, Hassan Z, Nukala S, Somagutta MR, Hamid P. Overview of risk factors and prevention of capsular contracture following implant-based breast reconstruction and cosmetic surgery: A systematic review. *Cureus*. 2020;12(9):e10341.
21. Bachour Y, Bargon CA, de Blok CJM, Ket JCF, Ritt M, Niessen FB. Risk factors for developing capsular contracture in women after breast implant surgery: A systematic review of the literature. *J Plast Reconstruct Aesthet Surg*. 2018;71(9):e29–e48.
22. Steiert AE, Boyce M, Sorg H. Capsular contracture by silicone breast implants: Possible causes, biocompatibility, and prophylactic strategies. *Medic Dev*. 2013;6:211–218.
23. Safran T, Nepon H, Chu CK, et al. Current concepts in capsular contracture: Pathophysiology, prevention, and management. *Semin Plast Surg*. 2021;35(3):189–197.
24. Watad A, Rosenberg V, Tiosano S, et al. Silicone breast implants and the risk of autoimmune/rheumatic disorders: A real–world analysis. *Int J Epidemiol*. 2018;47(6):1846–1854.
25. Contant CM, Swaak AJ, Obdeijn AI, et al. A prospective study on silicone breast implants and the silicone-related symptom complex. *Clin Rheumatol*. 2002;21(3):215–219.
26. Lee IM, Cook NR, Shadick NA, Pereira E, Buring JE. Prospective cohort study of breast implants and the risk of connective-tissue diseases. *Int J Epidemiol*. 2011;40(1):230–238.
27. Saigusa R, Asano Y, Nakamura K, et al. Association of anti-RNA polymerase III antibody and silicone breast implants in patients with systemic sclerosis. *J Dermatol*. 2016;43(7):808–810.
28. Hajdu SD, Agmon-Levin N, Shoenfeld Y. Silicone and autoimmunity. *Eur J Clin Invest*. 2011;41(2):203–211.
29. Cohen Tervaert JW, Colaris MJ, van der Hulst RR. Silicone breast implants and autoimmune rheumatic diseases: Myth or reality. *Curr Opin Rheumatol*. 2017;29(4):348–354.
30. Ajdic D, Zoghbi Y, Gerth D, Panthaki ZJ, Thaller S. The relationship of bacterial biofilms and capsular contracture in breast implants. *Aesthet Surg J*. 2016;36(3):297–309.
31. Schreml S, Heine N, Eisenmann-Klein M, Prantl L. Bacterial colonization is of major relevance for high-grade capsular contracture after augmentation mammaplasty. *Ann Plast Surg*. 2007;59(2):126–130.
32. Villanueva KG, Barr ML, Klingbeil KD, Tranfield W, Festekjian J. The role of antibiotic prophylaxis in primary and secondary implant-based breast augmentation: A systematic review and meta-analysis. *Ann Plast Surg*. 2023;91(3):400–405.

33. Guimier E, Carson L, David B, Lambert JM, Heery E, Malcolm RK. Pharmacological approaches for the prevention of breast implant capsular contracture. *J Surg Res*. 2022;280:129–150.
34. Pereira Leite L, Correia Sá I, Marques M. Etiopathogenesis and treatment of breast capsular contracture. *Acta Med Port*. 2013;26(6):737–745.
35. Little G, Baker Jr JL. Results of closed compression capsulotomy for treatment of contracted breast implant capsules. *Plast Reconstr Surg*. 1980;65(1):30–33.
36. Forster NA, Künzi W, Giovanoli P. The reoperation cascade after breast augmentation with implants: What the patient needs to know. *J Plast Reconstruct Aesthet Surg*. 2013;66(3):313–322.
37. Maxwell GP, Gabriel A. The neopectoral pocket in revisionary breast surgery. *Aesthet Surg J*. 2008;28(4):463–467.
38. Maxwell GP, Birchenough SA, Gabriel A. Efficacy of neopectoral pocket in revisionary breast surgery. *Aesthet Surg J*. 2009;29(5):379–385.