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Advances on Capsular Contracture—Prevention and Management Strategies: A Narrative Review of the Literature

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Background: Capsular contracture (CC) is the most relevant complication of both aesthetic and reconstructive breast implant surgery. For many years, experimental and clinical trials have attempted to analyze CC risk factors, clinical features, and appropriate management strategies. It is commonly accepted that a multifactorial etiology promotes CC development. However, the heterogeneity in patients, implants and surgical techniques make it difficult to suitably compare or analyze specific factors. As a consequence, discordant data are present in literature, and a true systematic review is often limited in its conclusions. Hence, we decided to present a comprehensive review of current theories on prevention and management strategies, rather than a specific "solution" to this complication.
Methods: The PubMed database was searched for literature regarding CC prevention and management strategies. Pertinent articles in English, published before December 1, 2022, were compared with selection criteria and eventually included in this review.
Results: Through the initial search, 97 articles were identified, of which 38 were included in the final study. Several articles explored different medical and surgical preventive and therapeutic strategies, showing numerous controversies on appropriate CC management.
Conclusions: This review provides a clear overview of the complexity of CC. The wide variety of clinical situations in term of patients, implants, and surgical techniques prevent the standardization of CC management strategies. By contrast, a patient-customized approach should be preferred, and different strategies should be considered depending on the specific case. Further research is desirable to better ascertain evidence-based protocols with regard to CC prevention and treatment.
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INTRODUCTION

Accounting for more than 1.2 million procedures worldwide each year, breast implant placement represents one of the most popular procedures within aesthetic and reconstructive surgery.[1,2] When a breast implant is set, the immune system reacts physiologically by forming a thin fibrous capsule, which stabilizes the implant in place. The capsule normally does not exceed 1–1.5 mm,[3,4] but in some cases, it undergoes a pathological fibrotic thickening process, leading to capsular contracture (CC).[5] CC develops from a few months to several years after implant surgery.[6]

CC incidence is heterogenous. Data range from 2.8% to 20.4% between 5 and 10 years after breast augmentation,[7–9] and up to 30% at 3 years in cases of reconstruction.[9] Discordant data result as a lack in standardization in implants choice and surgical techniques.[5,10] Most authors agree on a multifactorial etiology of CC, yet discordant reports award greater importance to different risk factors.[11,12] Biofilm, injuries, hematomas, type of implant, silicone leakage, surgical incision, individual susceptibility, and propensity for hypertrophic scarring are thought

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Table 1. The Baker Classification

Grade I	The breast is normally soft and looks natural
Grade II	The breast is a little firm but looks normal
Grade III	Visible distortion: the breast is firm and looks abnormal
Grade IV	Greater distortion: the breast is hard, painful, and looks abnormal

to play a major role in its development.[13–15] Radiotherapy itself is associated with a 50% to 70% increase in CC incidence.[13,14] Increase in breast firmness, hard breast, and breast pain eventually associated with visible distortion is the typical clinical presentation of CC. Standard evaluation relates to the Baker classification introduced by Baker in 1978[16] (Table 1). Patients with Baker Class III and IV typically require intervention. Proper treatment is still an open debate.

With this article, we reviewed the most recent research on CC prevention and treatment. Current approaches to the management of this complication are discussed as follows.

MATERIAL AND METHODS

A PubMed search was carried out using the terms "breast implant," "capsular contracture," "capsular contracture AND prevention," "capsular contracture AND risk factors" and "capsule contracture AND implant size." A manual search of study references was also performed. Studies were excluded using the following criteria: studies not written in English, communication letters, case reports, animal studies, studies not relevant to CC diagnosis and management strategies, and review articles. Pertinent studies in English published up to December 1, 2022 were included in this review.

RESULTS

The primary search yielded a total of 1877 articles, which were assessed for relevance based on their title and abstract. As a result, 97 articles were compared against the exclusion criteria, of which 43 were then fully reviewed, and 38 included and used in the synthesis of the information presented in this review (Fig. 1). The publications were categorized based on whether they aimed to describe CC risk factors and prevention (19) (Supplemental Digital Content 1), or management strategies (19) (Supplemental Digital Content 2). (**See table, Supplemental Digital Content 1,** which shows clinical evidence for risk factors and prevention of CC. **http://links.lww.com/PRSGO/C608**.) (**See table, Supplemental Digital Content 2,** which shows clinical evidence for the appropriate treatment of CC. **http://links.lww.com/PRSGO/C609**.)

DISCUSSION

Pathogenesis

Researchers agree of CC multifactorial origin.[17] Patient characteristics, implant factors and surgical techniques are known to influence on host immune response, which seems to be the real CC causative agent.[17] A schematic mechanism is represented in Figure 2. The periprosthetic chronic inflammation may drive a progressive fibrotic thickening process leading to CC.[10,18,19] Macrophages, cytokine, and cellular mediators such as IL 8 and TNF-α and transforming growth factor sustain the local inflammation,[20,21] adhesion, and fibrosis.[22]

A recent study has also demonstrated a direct association between capsular fibrosis and hypoxia.[23] The implant is avascular, and the neighboring area encounters relatively hypoxic conditions. Hypoxia may enhance tissue release of hypoxia-inducible factor-1 (HIF-1), increase levels of extracellular matrix (ECM)-associated factors, and promote epithelial-mesenchymal transition of the periprosthetic tissues.[23] Epithelial-mesenchymal transition seems to be a predominant source of myofibroblasts,[24,25] and their concentration has been directly associated with contracture severity.[26] HIF-1 may become a new pharmacological target, and future research should take this finding into consideration.

Takeaways

Question: Capsular contracture: where are we now and what are the future prospects?

Findings: The heterogeneity in patients, implants, and surgical techniques make it difficult to suitably compare or analyze specific factors. As a consequence, discordant data are present in the literature, and a true systematic review is often limited in its conclusions. Hence, we decided to present a narrative review of current theories on prevention and management strategies.

Meaning: The wide variety of clinical situations prevent the standardization of capsular contracture management strategies. By contrast, a patient-customized approach should be preferred, and different strategies should be considered depending on the specific case.

Risk Factors

Patient Factors

Genetics and individual susceptibility could promote exaggerated immunological response and periprosthetic inflammation.[27,28] The correlation is well known with hypertrophic scarring; however, little is known about CC.[11] In addition, within patient factors, recent research has highlighted a possible role of pregnancy.[29] Pregnancy induces breast increase in vascularization and trophism.[29] The vascularity increase has been associated with a higher risk of hematoma formation and may precipitate CC.[29]

Radiotherapy

Postmastectomy radiation therapy is a strong profibrotic risk factor. Data show up to a 50% increase risk of CC in patients who undergo breast postmastectomy radiation therapy and silicone implant breast reconstruction over nonirradiated reconstructions.[30,31] In particular, postmastectomy radiation therapy promotes scarring of the pectoralis major muscle, pain, and implant displacement.[32] A recent study identified radiotherapy-related

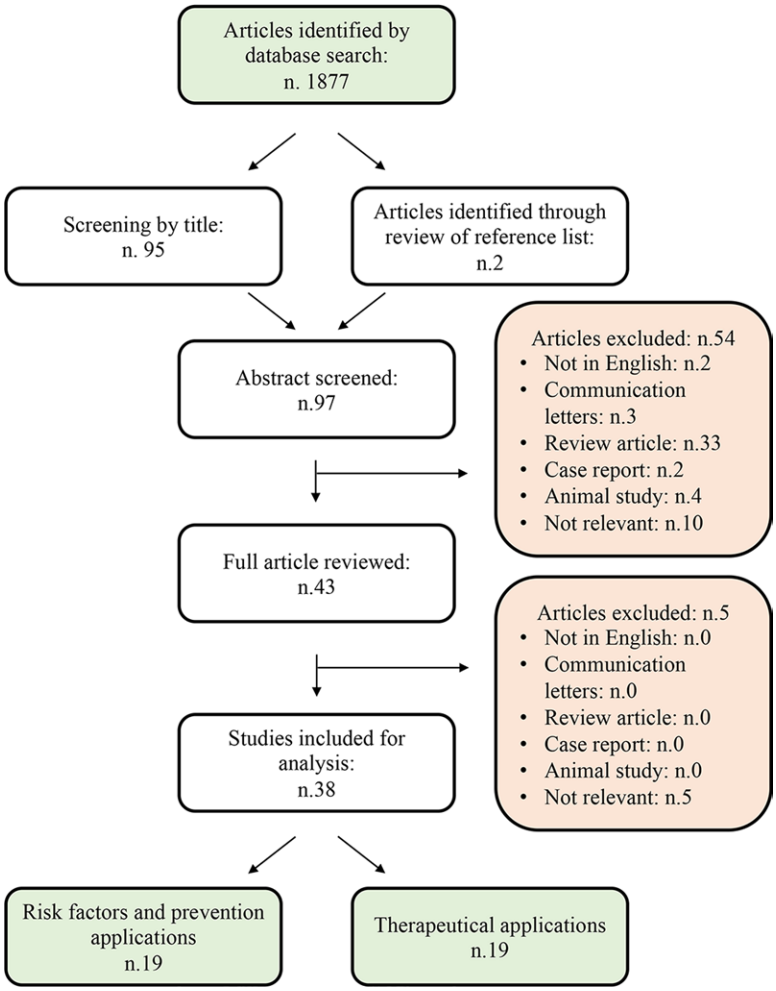

Fig. 1. Flow diagram summarizing the research results.

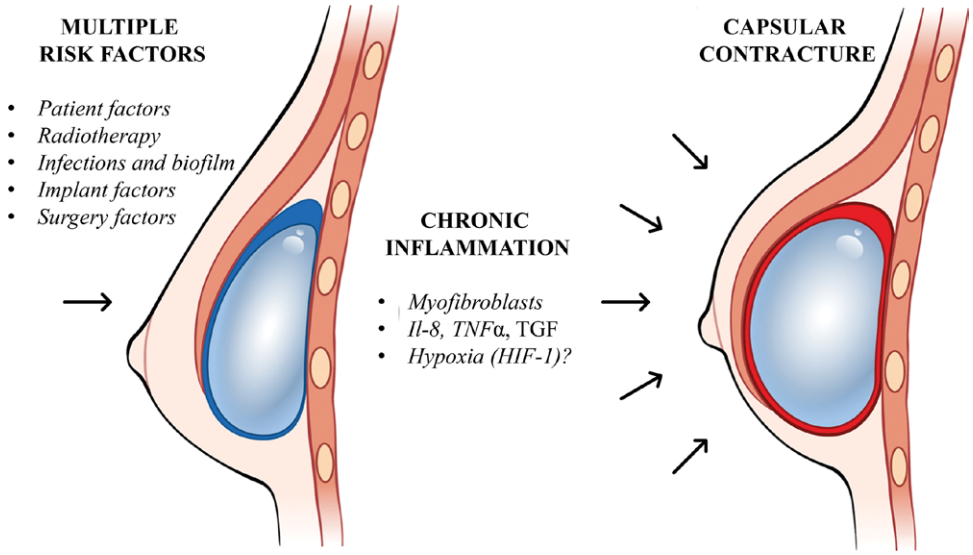

Fig. 2. CC pathogenesis schematic model.

activation of myofibroblasts with overexpression of the Thy1 protein (also called CD90). The study has also shown that in vitro Thy1 targeting with salinomycin has an interesting anti-scarring ability that should be further explored with in vivo studies.[33]

Infections and Biofilm

The association between subacute peri-prosthetic infection and CC is well known, and surgeons routinely use antiseptic preparations to wash the implant and irrigate the pocket during surgery.[34–36] *Propionibacterium acnes*, *E. coli*, and *Staphylococcus epidermidis* are the most frequently implicated agents.[34–36] Minimizing skin contact reduces the risk of CC, but contamination may still occur, as *Staphylococcus epidermidis*, a common part of the skin flora, has also been identified as part of the endogenous flora of the breast.[35,37]

Different types of pocket irrigation have been studied,[38] and data show that saline irrigation is associated with a higher risk of CC compared with antibiotic irrigation.[38] It is noteworthy that the United States Food and Drug Administration in 2000 banned implant instillation with povidone-iodine, due to the increased risk of implant deflation.[39] The ban was later revoked in 2017.[40] Venkataram et al[41] studied both the Betadine and non-Betadine antibiotic regimens, with the Betadine regimen being preferred. In particular, Betadine was preferred due to its greater coverage on Gram-negative bacteria.[41] Overall, infection prevention is critical in CC prevention, yet specific protocols should be further investigated.

Implant Factors

Since Thomas Cronin and Franck Gerow first used a silicone implant in 1962, continuous refinement and optimization of implant materials has led to numerous improvements in both aesthetic results and surgical safety.[42] Nowadays, implant-based breast surgery may rely on a wide variety of implants. These can be primarily summarized depending on their main characteristics: silicone gel or saline solution filling, smooth or textured surface and round or anatomical shape.[5] Size, of course, may change as well. Different implants have slightly different properties regarding CC formation and therefore have been investigated by several studies.[43–47]

Silicone Gel versus Saline

Saline and silicone gel filled implants are both characterized by an outer silicone shell.[48] Saline implants can be inserted through a small incision and subsequently filled with saline at surgery; however, any eventual breach in the shell would result in instant deflation of the implant.[48] Silicone gel filled implants have a much more natural consistency because of the viscosity of the filler.[49] However, old-generation silicone implants have been associated with implant rupture[48] and silicone bleeding, which is a strong CC trigger.[50] New-generation silicone implants are realized with a much more viscous and cohesive gel that prevents silicone leakage, therefore reducing CC risk. Caplin et al[51] investigated MemoryGel breast implant safety. These new-generation implants consist of a single-lumen, round silicone elastomer shell, with a patch on the posterior side, and are filled with a cohesive silicone gel. CC rate was identified as 12.1% for primary augmentation and 24.4% for primary reconstruction; low rupture rates were identified as well.[51] Nowadays, it is unanimously accepted that new-generation silicone implants should be preferred.[47,52]

Smooth versus Textured

Implant surfaces modulate implant-tissue interface, which is critical in CC development.[53] Textured surface implants carry a lower CC risk.[34,54–58] The surface pores of textured implants seem to promote fibroblast deep random arrangement[59] and force vectors deviation.[14,60–62] Conversely, smooth implants allow for the fibroblasts within the capsule to align parallel to the implant surface, readily allowing for contraction.[60,61,63]

However, textured implants carry a higher risk of BIA-ALCL,[64,65] and a higher rate of cancer recurrence in breast oncologic reconstruction surgery.[66] New micro and nanotextured implants have come to the market as a possible solution.[67,68] The goal is to maintain a texturization, but balance oncological concern.[69] New implant biocompatibility improvement may reduce CC risk as well as other complications such as seroma, hematoma, and rippling.[69]

Size and Shape

Implant size and shape may affect CC risk by modulating tissue mechanical interactions.[70] Available literature has shown contradictory results. Implants greater than 350 cm^3 have been associated with a higher CC incidence,[71] but other authors could not confirm the association.[29] By contrast, a biochemical study designed by making use of basic elasticity theories demonstrated a counterintuitive amplified stress field at the capsule-implant interface for small-size implants.[70] Other researchers have identified a reduction in CC recurrence when a lower volume implant is applied in place of a larger volume one.[72] For what concerns shape and CC association, we could not find any significative study.

Surgery Factors

Surgical choices include incision site selection, implant type, implant pocket location,[73] skin preparation strategies,[73,74] and eventual antiseptic breast pocket irrigation.[73] Preventive approaches should include proper prophylactic antibiotics, minimal-touch handling of the implant, strict respect for sterility, change of surgical gloves, and minimal time of implant opening.[73,75]

Surgery Incision Accesses

Incision accesses include inframammary, periareolar and transaxillary.[76] Collected data show that the inframammary incision results in lower CC rates.[73,77] The presence of bacterial flora in the ductal systems could account for the increased risk of CC in the periareolar access.[78,79] However, patients with larger areolas may still benefit from it.[80] The transaxillary incision has been associated with increased risk of implant malposition, secondary

procedures, and hematoma, which may precipitate CC.[81] However, the endoscopic assisted transaxillary approach seems to lower complications by minimizing bleeding and surgical trauma.[82]

Breast Implant Placements

Traditionally, implant placements include submuscular[83–85] and subglandular placement.[86,87] An epidemiological study reports CC incidence rates of 1.9% and 9.6%, respectively.[88] The submuscular placement isolates the implant from the endogenous flora of the glandular tissue.[35,37] It also reduces mechanical friction in the surrounding tissues.[17] Implants might also be located dual plane[86] by creating a plane of surgical dissection between the subglandular tissue and the pectoralis major fascia.[86] This approach appears to promote retraction of the upper parenchyma, thus reducing breast ptosis.[86] However, in a multicenter retrospective clinical study performed in Italy from January 2010 to June 2018 on 716 direct-to-implant reconstructions,[89] dual plane reconstruction was associated with a CC rate of 13.87% versus 8.7% for prepectoral placement.

Surgical choices also include subfascial placement, which involves placing the breast implant under the prepectoral fascia and over the pectoralis muscle.[90,91] This technique may avoid the pain and complications associated with submuscular pocket dissection, while still providing the benefits of subfascial placement such as lower CC frequency and lower implant visibility.[92,93] Proper indications include thin and athletic patients, as subfascial placement preserves the pectoral muscle.[92,93] Kerfant et al[94] conducted a study on 156 cases describing a CC rate of 3.85% with a mean follow-up period of 22.5 months. In another study on 200 cases, Brown et al[93] found an even lower CC rate, estimated at 0.5%. In the light of these considerations, further comparative studies on the different techniques should be carried out.

CC Diagnosis

CC diagnosis and severity evaluation traditionally relies on clinical examination based on a subjective classification system proposed by Baker in 1978[16] (Table 1) and integrated by Spear and Baker with categories IA/B for palpable and nonpalpable implants in soft breasts.[16] However, this approach prevents a standardized assessment of the disease and its severity, and consensus is not present among surgeons. As a possible solution to this concern, ultrasound examination has been proposed.[95]

Zuniga et al[96] aimed to correlate ultrasound findings, such as an increased number of radial folds, calcification areas, abnormal wrinkles, and deformation of the implant,[97] with CC severity. A total of 21 patients with smooth surface contracted implants were included. When comparing breasts graded Baker I to IV, a mean capsule thickness of 0.6±0.2, 1.0±0.53, 1.68±0.99, and 1.52±0.46 mm, respectively, was shown. A similar correlation was also described by Kim et al.[98] The author reported that a capsule thickness of 0.4–0.8 mm, 0.8–1.31 mm, and 1–4.1 mm was associated with Baker grades II, III, and IV, respectively. Ultrasound may provide a rapid, effective, noninvasive, and replicable test for CC severity assessment. It is hoped that future studies will validate these findings.

CC Surgical Treatment

Most authors agree that the gold standard of CC treatment is represented by capsulectomy, site change, and implant exchange.[15,99,100] Success rate is estimated at 79%, but the procedure carries morbidity, and it is not free from complications.[101] It is also technically more complicated than capsulotomy, which involves incision and release of the pathological capsule, or partial capsulectomy in which the fibrotic capsule is only partially dissected and removed.[102] Recurrence rate studies have shown similar results between techniques ranging from 0% to 54%,[99] thus opening the debate.

Implant replacement, with or without implant site change, is essential in CC recurrence prevention, as it guarantees any biofilm removal.[99,102] When changing the implant, smooth or textured implants can be chosen, and consensus is not present.[71,102] Capsulotomy and partial capsulectomy do not completely remove the fibrotic capsule, and the remaining parts could act as an instigator for CC recurrence.[102] Literature suggests that different clinical situations may benefit from different treatments.[71,102,103] If the contracted implant is in a premuscular pocket, capsulectomy, implant exchange, and site change into a sub-muscular pocket should be preferred.[103] If the first implant placement was sub-muscular, partial capsulectomy or capsulotomy should be considered for less surgical trauma, bleeding, and complications risk.[104] Capsulotomy is indicated when replacing a saline implant, as the capsule of these implants typically disappears within 1 year of removal.[102] Partial capsulectomy represents a great compromise between total capsulectomy, which carries important scarring and hematoma risk, and capsulotomy, which does not include capsule removal,[105] and it could potentially become the new standard of treatment for CC.[106]

New Possible Preventive Strategies

Autologous Fat Transfer

The surgeon can place a fat graft in the initial procedure and use lipofilling as an alternative CC treatment. Data showed that lipofilling was effective in ameliorating pain from capsular formation, as it reduced the foreign body sensation, the feeling of tension, and the feeling of cold breast.[107] Haran et al[108] showed that fat grafting elevated the CC resolution rate of secondary procedures up to 86%.[108] Overall, CC treatment with autologous fat transfer, possibly associated with surgery, may represent an innovative procedure, and further studies should be performed.[109]

Acellular Dermal Matrix

Acellular dermal matrix (ADM) is a biotechnological tissue prepared from human, porcine, or bovine components.[110] The tissue is modified by removing cells and inflammatory components. The result is an inert matrix that provides support for physiological tissue ingrowth,

cellular repopulation, and revascularization.[110,111] When ADM is used in implant breast surgery, it provides additional coverage of the implant, especially in the inferolateral pole where the pectoralis muscle is lacking.[112,113] It also offers an additional layer of tissue between the skin and the implant.[110,111] Researchers hypothesized that ADM may reduce CC recurrence rate, and several clinical studies showed encouraging results.[114–116] However, other studies reported ADM association with a higher risk of seroma and pocket infection; moreover, the expensive cost of the procedure limits a wide use.[117]

As a possible solution to minimize ADM costs, new bioabsorbable meshes have been studied. GalaFLEX is a biosynthetic meshes that derives from a linear polyester produced by recombinant fermentation.[118] The mesh is designed with strong fibers, which help tissue ingrowth and minimize infections; it is fully absorbed in 18–24 months.[118] Singalove et al[119] compared safety of using GalaFLEX-AlloDerm construct in 128 patients (249 breasts) versus AlloDerm alone in 135 patients (250 breasts) in prepectoral reconstructions. In GalaFLEX-AlloDerm reconstructions, the lower third of the expander was covered by the AlloDerm, whereas the rest of the expander was covered by GalaFLEX, thus requiring much less AlloDerm. The rate of CC did not differ significantly between groups, and it was less than 3.0%. An alternative solution may be represented by Durasorb. Durasorb is a resorbable polydioxanone mesh designed with macro-porous monofilament which promote rapid tissue incorporation.[120] Turin et al[120] evaluated its efficacy in revisional breast surgery describing 17 patients (27 breasts) with no infections, wound healing problems, or recurrences of implant malposition/CC encountered with an average follow-up of 355 days. In light of these considerations, GalaFLEX and Durasorb may represent equally effective and less expensive devices than ADM.

CONCLUSIONS

This narrative review of the literature has attempted to outline some of the recent research on CC prevention and management strategies. From the current review, surgery seems to represent the most effective therapeutic approach to CC. Surgeons should be able to perform different techniques and manage different implants and innovative procedures as a proper approach to the wide variety of clinical situations. The next challenge, in our perspective, is to further acknowledge a "personalized approach" in which the treatment is customized to the patient, and future research is desirable to achieve such an ambitious target.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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