Since the first reported case in 1997, breast implant–associated anaplastic large-cell lymphoma (BIA-ALCL) has been a difficult entity to characterize because of its low incidence and understated clinical course, but studies have begun to shed light on its pathogenesis, diagnosis, and management. It is now understood that BIA-ALCL is a rare form of non-Hodgkin lymphoma that has been associated with textured breast implants. Textured surfaces are thought to induce

**Background:** Although guidelines have been published on treatment of breast implant–associated anaplastic large-cell lymphoma (BIA-ALCL), there has been no comprehensive analysis of BIA-ALCL treatment variation based on the available literature. The authors sought to assess current treatment strategies of BIA-ALCL relative to current guidelines.

**Methods:** Database searches were conducted in June of 2020. Included articles were case reports and case series with patient-level data. Collected variables included clinicopathologic features, implant characteristics, diagnostic tests, ALCL characteristics, treatment, and details of follow-up and outcome. Treatment data from before and after 2017 were compared with National Cancer Center Network guidelines.

**Results:** A total of 89 publications were included and 178 cases of BIA-ALCL were identified. Most patients presented with seroma (n = 114, 70.4 percent), followed by a mass (n = 14, 8.6 percent), or both (n = 23, 14.2 percent). Treatment included en bloc capsulectomy of the affected implant in 122 out of 126 cases with treatment details provided (96.8 percent). Radiation therapy was given in 38 cases (30.2 percent) and chemotherapy was given in 71 cases (56.3 percent). Practitioners used less chemotherapy for local disease after treatment guideline publication in 2017 (p < 0.001), whereas treatment for advanced disease remained unchanged (p = 0.3). There were 10 recurrences and eight fatalities attributable to BIA-ALCL, which were associated with advanced presentation (29 versus 2.1 percent; OR, 19.4; 95 percent CI, 3.9 to 96.3; p < 0.001).

**Conclusions:** BIA-ALCL remains a morbid but treatable condition. Current guidelines focus treatment for local disease and reduce nonsurgical interventions with radiation or chemotherapy. Patients presenting with advanced BIA-ALCL experience higher rates of recurrence and mortality. (Plast. Reconstr. Surg. 150: 762, 2022.)

**Disclosure:** Dr. Fischer has received payments as a consultant for Baxter, Becton-Dickinson, W. L. Gore, and Integra Life Sciences. No financial support was received for this study. The other authors have no financial interest to declare in relation to the content of this article.

Related digital media are available in the full-text version of the article on www.PRSJournal.com.
a chronic inflammatory state that may induce malignant transformation of T cells in susceptible patients. Most cases present as a local periprosthetic effusion and local disease is virtually curable with early treatment. BIA-ALCL is thought to be an indolent disease, but it is crucial to recognize it early, because deaths have been reported in very advanced cases. While once thought to be rare, recent studies have suggested the true incidence may be higher than early epidemiologic estimates.

Treatment of BIA-ALCL has been highly variable, using both surgical and nonsurgical interventions. Lack of consensus led to individualized treatment regimens based on expert opinions. In 2017, the National Cancer Center Network released landmark guidelines that provided an algorithmic approach to diagnosis and treatment of BIA-ALCL. Based on these guidelines, surgical intervention with implant removal and en bloc capsulectomy ensures optimal outcomes in all patients with BIA-ALCL, whereas systemic therapy is appropriate for more advanced cases.

National and international efforts to create BIA-ALCL registries have resulted in more robust database studies, but many cases are missed by these registries and are instead published as case reports. Given the improved understanding of BIA-ALCL diagnosis and management, the authors sought to provide an updated systematic review of the case literature on BIA-ALCL to help characterize treatment variation in relation to National Cancer Center Network guideline publication.

Methods

Search Strategy

This systematic review was registered on PROSPERO (identification no. CRD42020197585) and conducted in accordance with the Preferred Reporting Items for a Systematic Review and Meta-Analysis checklist and Meta-analysis of Observational Studies in Epidemiology group guidelines. Database searches were conducted in June of 2020 to identify material written on breast implants and anaplastic large-cell lymphoma. In consultation with all authors, a medical librarian (F.M.C.) developed individual search strategies (see Figure, Supplemental Digital Content 1, which shows Preferred Reporting Items for a Systematic Review and Meta-Analysis Flow Diagram, http://links.lww.com/PRS/F341) and retrieved citations from PubMed, EMBASE, Scopus, and Cochrane Library. A combination of the following text words and controlled vocabulary terms was used: “breast implants,” “mammaplasty,” “breast reconstruction,” “anaplastic large-cell lymphoma,” “ALCL,” “lymphoma,” and “seroma.” In addition, a search of grey literature (unpublished, noncommercial, difficult-to-find information produced by organizations such as professional associations, research institutes, think tanks, and government departments) was conducted using Google Scholar. All search results were limited to material published since 1999. After the final exclusion, bibliographies of included articles were collected and screened. No authors of searched articles were contacted throughout the course of this study.

Eligibility Criteria

Inclusion criteria encompassed the diagnosis of ALCL in patients 18 years of age or older with at least one breast implant. Included articles were case reports and case series with patient-level data. Excluded articles were retrospective and prospective cohort studies, review articles, editorials, commentaries, and abstracts. Using Covidence systematic review management software, two authors (J.A.M., H.I.N.) independently reviewed the abstract and, if necessary, the full text of all search results for inclusion and exclusion criteria. Discrepancies between authors were resolved through discussion with the senior author (J.P.F.).

Data Extraction, Outcomes of Interest, and Synthesis of Evidence

Predefined variables were extracted independently by study authors (M.P.M., A.N.C., J.A.M., H.I.N.), and any discrepancies were reconciled by the study team. Collected variables included clinicopathologic features (age at presentation, initial presenting symptom, indication for implant, breast cancer history, time from implant to presentation), implant characteristics (surface, type, manufacturer), diagnostic tests (radiologic, pathologic), ALCL characteristics (laterality, staging), treatment (implant removal, capsulectomy, axillary node excision, radiation, chemotherapy), and details of follow-up and outcome (duration of follow-up, recurrence, fatality). Staging data and treatment data were compared with 2017 National Cancer Center Network Consensus Guidelines using a date of publication before or after 2017 to denote preguideline or postguideline publication. Staging was defined using TNM (tumor, lymph node, metastasis) classification when available in the included articles. Local disease was
defined as TNM IA through IC and advanced disease was defined as TNM II through IV based on National Cancer Center Network guidelines. Cases without staging data were excluded from analysis. Data were pooled and represented as collective data points using descriptive statistics. For each variable of interest, the denominator used was defined as the number of cases that reported the variable, not the total number of cases. The Fisher exact test was used to compare categorical variables, as appropriate. Univariate statistical significance was set at $p < 0.05$. Statistical calculations and analyses were performed using STATA version 12 (StataCorp, College Station, Texas).

**RESULTS**

**Clinicopathologic, Implant, and Radiologic Characteristics**

A total of 89 case reports or series and 178 patients were included. (See Supplemental Digital Content 1, which shows the list of case reports used for data collection, http://links.lww.com/PRS/F341). Descriptive statistics can be found in Table 1. Median age at presentation was 53 years (interquartile range, 45 to 61 years). A total of 114 patients (70.4 percent) presented with seroma, 14 patients (8.6 percent) presented with a mass, 23 patients (14.2 percent) presented with both, and 11 patients (6.8 percent) presented with various other symptoms or physical examination findings, including capsular contracture, B symptoms, and lymphadenopathy, among others. No data on initial presentation were available for 14 cases. A total of 90 patients (56.6 percent) had implants placed for cosmetic augmentation and 69 patients (43.4 percent) underwent implant-based reconstruction; 19 cases had no information regarding reason for implant placement. A total of 52 patients (37.7 percent) had a reported breast cancer history before initial implant placement. Median time from implant to presentation was 9 years (interquartile range, 4.75 to 13.75 years). A total of 88 implants (69.8 percent) were silicone-filled and 38 were saline-filled (30.2 percent); 52 cases did not report type of implant. Implant surface was reported in 93 cases, all of which had textured surfaces. The most common implant manufacturers reported are summarized in Table 2. Most implants were manufactured by Allergan (Dublin, Ireland) ($n = 51$, 79.7 percent), followed by GC Aesthetics (Dublin, Ireland) ($n = 8$, 12.5 percent). The implant manufacturer was not mentioned in 114 cases.

The most common diagnostic radiographic tests performed were ultrasound ($n = 90$, 71.1 percent) and positron emission tomography and computed tomography ($n = 81$, 76.5 percent). Pathologic tests included cytology in 110 cases and immunohistochemistry in 125 cases. The majority of BIA-ALCL cases were unilateral ($n = 110$, 96.4 percent) and very few were bilateral ($n = 4$, 3.5 percent); 64 cases did not report BIA-ALCL laterality. A total of 127 (100 percent) of reported cases were confirmed to be CD30+/ALK−; others did not mention immunohistochemistry status.

| Table 1. Descriptive Results* |
| Variables ($n =$ Cases with Available Data) | Values |
| Clinicopathologic characteristics | |
| Age at presentation, yrs | $53 \pm 8$ |
| Initial presentation ($n = 162$) | | |
| Seroma | 114 (70.4) |
| Mass | 14 (8.6) |
| Both | 23 (14.2) |
| Other | 11 (6.8) |
| Time from implant to presentation | $9 \pm 4.75$ |
| Breast cancer history ($n = 138$) | 52 (37.7) |
| Staging | |
| Confined to capsule (TNM IIA through IIC) | 49 (73.1) |
| Mass (TNM IIA) | 13 (19.4) |
| Advanced disease (TNM IIB through IV) | 5 (7.46) |
| Treatment | |
| Removal of affected implant ($n = 126$) | 121 (96.0) |
| Removal of contralateral implant ($n = 89$) | 69 (77.5) |
| En bloc capsulectomy ($n = 137$) | 130 (94.9) |
| Axillary node excision ($n = 89$) | 13 (14.6) |
| Radiation ($n = 121$) | 38 (31.4) |
| Chemotherapy ($n = 132$) | 71 (53.8) |
| Number of cycles | $6 \pm 2$ |
| Follow-up | |
| Clinical follow-up reported | 128 (74.0) |
| Duration of follow-up, months | $22.5 \pm 20.9$ |
| Recurrence | 10 (7.8) |
| Fatal | 8 (6.25) |

*Values are expressed as mean ± SD or n (percent of cases with available data).

| Table 2. Implant Characteristics* |
| Variables ($n =$ Cases with Available Data) | Values |
| Indication for implant ($n = 159$) | |
| Prophylactic mastectomy/reconstruction | 69 (43.4) |
| Cosmetic | 90 (56.6) |
| Implant laterality ($n = 84$) | |
| Left | 5 (6.0) |
| Right | 5 (6.0) |
| Bilateral | 74 (88.1) |
| Implant surface ($n = 93$) | |
| Textured | 95 (100) |
| Smooth | 0 (0) |
| Type of implant ($n = 126$) | |
| Silicone | 88 (69.8) |
| Saline | 38 (30.2) |
| Implant manufacturer ($n = 64$) | |
| Allergan (McGhan, Inamed, CUI) | 51 (79.7) |
| GC Aesthetics (Nagor, Eurosilicone) | 8 (12.5) |
| Salimed | 3 (4.7) |
| Mentor | 2 (3.1) |

*Values are expressed as n (percent of cases with available data).
Staging was stratified by local disease (TNM IA through IC; n = 50, 73.5 percent) or advanced disease (TNM II through IV; n = 18, 26.5 percent), but most cases did not have staging data.

Treatment Modalities and Comparisons to Standard of Care

Treatment included implant removal and en bloc capsulectomy in 122 out of 126 cases (96.8 percent). Removal of contralateral implant occurred in 69 out of 89 reported cases with bilateral implants (77.5 percent). Axillary node excision occurred in 13 cases (10.3 percent). Radiation therapy was administered in 38 cases (31.4 percent) and chemotherapy was given in 71 cases (53.8 percent). The most common chemotherapy regimens were CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) [44 patients (75.9 percent)], R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) [four patients (6.9 percent)], EPOCH (etoposide, vincristine, doxorubicin, cyclophosphamide, and prednisone) [four patients (6.9 percent)], and brentuximab vedotin [four patients (6.9 percent)]. Other regimens included V-EPOCH (bortezomib, etoposide, vincristine, doxorubicin, cyclophosphamide, and prednisone) [one patient (1.7 percent)], ABVD (adriamycin, bleomycin, vinblastine, and dacarbazine) [seven patients (11.7 percent)], DHAOX (dexamethasone, cytotoxic, and oxaliplatin) [one patient (1.7 percent)], and hyper-CVAD (hyper-fractionated cyclophosphamide, vincristine, doxorubicin, and prednisolone) [one patient (1.7 percent)]. Other adjuvants were rarely reported but included ICE (ifosfamide, carboplatin, etoposide, and mesna) in four cases and methotrexate in one, among others. Seven patients received stem cell transplants.

Subanalysis of treatment by BIA-ALCL stage revealed nuances in treatment strategies. For the 50 patients with reported local disease (TNM IA through IC), 35 patients (71.4 percent) were treated with implant removal and en bloc capsulectomy only; seven (14.3 percent) with implant removal, en bloc capsulectomy, and chemotherapy; three (6.1 percent) with implant removal, en bloc capsulectomy, and radiotherapy; and five (10.2 percent) with implant removal, en bloc capsulectomy, chemotherapy, and radiotherapy. For the 18 patients with reported advanced disease (TNM II through IV), three (16.7 percent) were treated with implant removal and en bloc capsulectomy only; nine (50 percent) with implant removal, en bloc capsulectomy, and chemotherapy; none with implant removal, en bloc capsulectomy, and radiotherapy; four (22 percent) with implant removal, en bloc capsulectomy, chemotherapy, and radiotherapy; and two (11 percent) with other regimens, which were chemotherapy and radiotherapy without en bloc capsulectomy (Fig. 1).

Analysis of treatment modalities before and after 2017 (which correlates with National Cancer Center Network guideline publication) revealed significant differences. For local disease, treatment in cases before 2017 tended to be more aggressive; 17 cases (58.6 percent) were treated with implant removal and en bloc capsulectomy only and 12 cases (41.4 percent) were treated with implant removal, en bloc capsulectomy, and chemotherapy. After 2017, 21 cases (100 percent) were treated with implant removal and en bloc capsulectomy only, and no cases were treated with implant removal, en bloc capsulectomy, and chemotherapy (Table 3). Before 2017, three cases of advanced disease were treated with implant removal and en bloc capsulectomy only and 12 cases were treated with implant removal, en bloc capsulectomy, and chemotherapy. After 2017, all 15 cases of advanced disease were treated with implant removal, en bloc capsulectomy, and chemotherapy (Table 4). Use of systemic chemotherapy for treatment of local BIA-ALCL was significantly associated with presentation before 2017 (p<0.001); there was no association between guideline publication and treatment variation for advanced BIA-ALCL (p = 0.31). In regard to adjuvant chemotherapy, 32 patients were treated with CHOP or brentuximab vedotin before 2017, versus 16 after 2017. Other chemotherapy regimens were used in six cases before 2017 and in two cases after 2017. There was no association between guideline publication and type of chemotherapy regimen used (p = 0.72) (Table 5).

Clinical follow-up was reported in 128 cases, with a mean follow-up duration of 22.5 ± 20.9 months. Recurrence occurred in 10 cases (7.8 percent), and eight patients (6.3 percent) died from complications of BIA-ALCL. Details of recurrence site were only reported in four cases, with one case of recurrence at the previous site of the breast capsule and three cases of distant recurrence outside of the capsule. Of the patients with recurrent disease, two patients initially presented with local disease (TNM IA through IC), seven patients initially presented with a mass (TNM IIA), and one patient initially presented with advanced disease (TNM IIB through IV). Treatment details for each recurrent case, along with other details about
Fig. 1. Overall treatment allocation by breast implant–associated anaplastic large cell lymphoma staging. "Surgery" denotes implant removal with en bloc capsulectomy. "Both" indicates both chemotherapy (Cx) and radiotherapy (Rx).

**DISCUSSION**

This study sought to summarize patient-level data on BIA-ALCL, provide an updated analysis of the association between presentation and recurrence and mortality, and analyze temporal trends in treatment strategies. To our knowledge, this is the largest systematic review of patient-level data to date. Descriptive aspects of the case literature were found to be consistent with previous studies with regard to disease presentation, implant surface type, time to diagnosis, and recurrence. However, the subanalysis of temporal trends in BIA-ALCL treatment strategies was particularly revealing. After National Cancer Center Network guideline publication in 2017, treatment patterns for local BIA-ALCL shifted significantly, favoring surgical therapy only (implant removal and capsulectomy) as opposed to local therapy with systemic chemotherapy or locoregional radiation therapy. This signifies a decrease in the provision of unnecessary chemotherapy, decreasing the systemic side effects and overall morbidity of treatment for patients with local disease. Conversely, treatment for advanced disease was not significantly recurrent cases, are available in Table 6. Adjusting for the one outlier of 144 months, mean time to recurrence after treatment was 14.6 ± 14.4 months. Recurrence or fatality was associated with mass at time of initial presentation (29 versus 2.1 percent; OR, 19.4; 95 percent CI, 3.9 to 96.3; \( p < 0.001 \)).

| Treatment type          | Local (TNM IA-IC) | Advanced (TNM II-IV) |
|-------------------------|-------------------|----------------------|
| Surgery only            | 35                | 3                    |
| Surgery w/ chemotherapy | 7                 | 9                    |
| Surgery w/ radiotherapy | 3                 | 0                    |
| Surgery w/ both         | 5                 | 4                    |
| Other                   | 0                 | 2                    |
associated with any change over time. This result is likely attributable to the fact that practitioners were already treating advanced BIA-ALCL aggressively with local therapy and chemotherapy before guideline publication. Overall, our results represent a shift in BIA-ALCL treatment for local disease.

With hundreds of thousands of breast implants placed every year, BIA-ALCL continues to warrant intense investigation and scrutiny as its overall rarity has caused debate about how practitioners should alter their breast implant–based practices. Many studies have attempted to estimate risk by reporting the incidence of BIA-ALCL, but an accurate estimate has been difficult to ascertain because of inconsistent global reporting of cases and inaccurate estimates of the total number of patients with breast implants. A study by Magnusson et al. revealed dramatically different incidences of BIA-ALCL stratified by textured surface type. In addition, they found that the incidence of BIA-ALCL in their population was increasing, which they attributed to improved awareness and detection. Nonetheless, textured implants continue to be used in various contexts worldwide. A 2018 report suggested that plastic surgeons have been incorporating more textured implants into their practices because of their advantages over smooth implants, including better stability within the implant pocket, lower rates of capsular contracture, and associated improved cosmetic outcomes. However, since 2015, authors have argued for the elimination of textured implants from practice, and many surgeons are asking themselves whether textured implant reconstruction is worth the risk of BIA-ALCL. In 2019, the U.S. Food and Drug Administration released a series of initiatives to garner better evidence about BIA-ALCL, but importantly, they did not ban macrotextured implants, citing insufficient evidence.

One trend becomes obvious upon appraising the literature: early diagnosis and treatment is essential to optimize outcomes in BIA-ALCL. A study in 2016 by Clemens et al. asserted the importance of complete surgical excision to ensure event-free survival in patients with BIA-ALCL. In comparison to partial capsulectomy, chemotherapy, or radiotherapy, complete surgical excision with implant removal was significantly associated with improved survival. They also found that extracapsular involvement was associated with worse survival. In this study, we found that

Table 3. Treatment Variation for Local BIA-ALCL (TNM IA through IC) before and after 2017*

| Treatment Type            | Before 2017 | After 2017 | p       |
|---------------------------|-------------|------------|---------|
| Surgery with chemotherapy | 12          | 0          | <0.001  |
| Surgery only              | 17          | 21         |         |

*Correlates with National Cancer Center Network BIA-ALCL guideline publication. "Surgery" denotes implant removal with en bloc capsulectomy.

Table 4. Treatment Variation for Advanced BIA-ALCL (TNM II through IV) before and after 2017*

| Treatment Type            | Before 2017 | After 2017 | p       |
|---------------------------|-------------|------------|---------|
| Surgery with chemotherapy | 7           | 8          | 0.31    |
| Other                     | 3           | 0          |         |

*Correlates with National Cancer Center Network BIA-ALCL guideline publication. Surgery denotes implant removal with en bloc capsulectomy.

Table 5. Variation of Chemotherapy Regimens in BIA-ALCL Treatment over Time

| Chemotherapy Regimen | Before 2017 | After 2017 | p   |
|----------------------|-------------|------------|-----|
| CHOP/brentuximab     | 32          | 16         | 0.72|
| Other                | 6           | 2          |     |

*Other regimens include R-CHOP, CVAD, CHOEP, and ABVD.

Table 6. Characteristics of Reported BIA-ALCL Recurrences in the Literature

| Case Number | Study Reference | Recurrence | Death | Staging† | Treatment | Time between Treatment and Recurrence (mo) | Notes |
|-------------|----------------|------------|-------|----------|-----------|----------------------------------------|-------|
| 1           | Letourneau et al. | Yes | No | Mass | Sx + Cx | 48 | |
| 2           | D’Alessandris et al. | Yes | Yes | Mass | Sx + Cx + Rx | 5 | |
| 3           | Laurent et al. | Yes | Yes | Mass | Sx + Cx | 7 | |
| 4           | Zimmerman et al. | Yes | Yes | Advanced | Sx | 2 | |
| 5           | Gaudet et al. | Yes | No/A | Mass | Sx | 12 | |
| 6           | Allidify et al. | Yes | Yes | Local | Sx | 144 | |
| 7           | Wu et al. | Yes | Yes | Local | Sx + Cx + Rx | 3 | |
| 8           | Carty et al. | Yes | Yes | Mass | Sx + Cx | 18§ | |

Cx, chemotherapy; Rx, radiation therapy; Sx, implant removal with en bloc capsulectomy.

*Reference citations are available in Document Supplemental Digital Content 2, http://links.lww.com/PRS/F342.

†“Advanced” indicates TNM II through IV. “Local” indicates TNM IA through IC. “Mass” indicates TNM IIA.

‡Death attributed to “lymphoma” but not specifically correlated with BIA-ALCL.

§Estimate of time to recurrence because of vague description.
presentation with a mass as opposed to a seroma was significantly associated with recurrence or mortality, with an odds ratio of 19.4 (95 percent CI, 3.9 to 96.3). We also found that recurrences were often treated appropriately with local and systemic therapies. This adds to the evidence that advanced disease is associated with significantly worse outcomes, emphasizing the importance of early detection. Nonetheless, surgical excision remains an effective treatment option regardless of cancer stage, as shown in a recent retrospective study. More recently, a prospective study by Tevis et al. found that 52 patients treated for BIA-ALCL achieved complete remission. This study is significant because it is one of the only prospective studies that evaluates BIA-ALCL outcomes and it indicates that timely comprehensive care can effectively cure BIA-ALCL.

Early implant removal and en bloc capsulectomy have become the standard of care for BIA-ALCL due to the aforementioned studies, but other treatments, such as chemotherapy and radiotherapy, have yet to be studied intensively. The National Cancer Center Network guidelines suggest adjuvant chemotherapy with either CHOP or brentuximab vedotin for advanced disease. CHOP is an anthracycline-based systemic therapy traditionally used for peripheral T-cell lymphomas. Brentuximab vedotin is an antibody–drug conjugate that binds to CD30, a marker that is highly expressed on malignant T cells in ALCL. These agents have yet to be studied thoroughly in BIA-ALCL, so their efficacy is based largely on case reports. In this study, we found that even before National Cancer Center Network guideline publication, the majority of practitioners had been using CHOP to treat BIA-ALCL. Although practitioners are using less chemotherapy overall in the treatment of local BIA-ALCL, their chemotherapy of choice has not changed over time.

Despite the strength of the aforementioned studies, there are no rigorous studies or trials to date that have comprehensively assessed BIA-ALCL treatment options. Most of the available literature that has guided BIA-ALCL treatment is based on either case reports or retrospective cohort studies. As such, prospective studies and reviews of the literature are critically needed to provide evidence for the most effective management of BIA-ALCL.

We consider our reliance on case reports to be a strength of our study, as the case literature catches cases not recorded in patient registries. However, the use of case reports leads to information gaps and thus to inconsistencies in the data collected. As such, this is also the largest weakness of our study. There were limited data on multiple parameters, including breast cancer history, BIA-ALCL staging, implant characteristics, recurrence, and fatality, among others. This limits the generalizability of our findings. Using case reports as opposed to cohort studies for data collection also underestimates the overall case numbers of BIA-ALCL. Larger studies that incorporate cohort studies may allow for more comprehensive analyses but would necessarily lack the granularity of specific patient data. In addition, using case reports likely overestimates the incidence of advanced disease and recurrence and fatality, as they are more likely to be reported than mild disease. Although we analyzed BIA-ALCL management in relation to National Cancer Center Network guideline publication, practitioner management patterns had likely already started shifting because of mounting evidence about BIA-ALCL management. The guidelines served as a matter of consensus that may have further shifted management patterns, although causality has yet to be established. In addition, we used 2017 as a time point for analysis; we acknowledge that there can be a lag time from when guidelines are published to when they are put into practice and then presented in downstream publications. We did not see evidence of this, however, suggesting that a change had already started to occur in management strategies before the guideline presentation.

Our results are encouraging, but more studies investigating the effects of treatment variation on long-term outcomes are needed. We were not able to provide an analysis of the association of treatment type with outcome because of low case numbers. Studies that prospectively follow BIA-ALCL, such as the study by Tevis et al., will more comprehensively define the implications of treatment variation in patient care. Furthermore, vigilant participation in PROFILE, the BIA-ALCL registry that is maintained by the American Society of Plastic Surgeons and the Plastic Surgery Foundation, is of critical importance to plastic surgeons as it provides a robust dataset to further BIA-ALCL investigations and ensure optimal outcomes.

CONCLUSIONS

BIA-ALCL continues to be primarily associated with textured implants and most often presents with local disease. We demonstrate that treatment for local disease was significantly less aggressive after treatment guideline publication in 2017.
Patients who presented with advanced disease had higher rates of recurrence and mortality.

John P. Fischer, M.D., M.P.H.
Division of Plastic Surgery
Department of Surgery
University of Pennsylvania Health System
51 North 39th Street
Wright Saunders Building
Philadelphia, Pa. 19104
john.fischer2@pennmedicine.upenn.edu
Twitter: @plasticfish83

REFERENCES

1. Keech JA Jr, Creech BJ. Anaplastic T-cell lymphoma in proximity to a saline-filled breast implant. Plast Reconstr Surg. 1997;100:554–555.
2. Kadin ME, Adams WP Jr, Inghirami G, Di Napoli A. Does breast implant-associated ALCL begin as a lymphoproliferative disorder? Plast Reconstr Surg. 2020;145:30e–38e.
3. Miranda RN, Ahedly TN, Prince HM, et al. Breast implant-associated anaplastic large-cell lymphoma: Long-term follow-up of 60 patients. J Clin Oncol. 2014;32:114–120.
4. Leberfinger AN, Behar BJ, Williams NC, et al. Breast implant-associated anaplastic large cell lymphoma: A systematic review. JAMA Surg. 2017;152:1161–1168.
5. Collett DJ, Rakhorst H, Lennox P, Magnusson M, Cooter R, Deva AK. Current risk estimate of breast implant-associated anaplastic large cell lymphoma in textured breast implants. Plast Reconstr Surg. 2019;143:405–10.
6. Nelson JA, Dabic S, Mehrara BJ, et al. Breast implant-associated anaplastic large cell lymphoma incidence: Determining an accurate risk. Ann Surg. 2020;272:403–409.
7. Cordeiro PG, Ghione P, Ni A, et al. Risk of breast implant associated anaplastic large cell lymphoma (BIA-ALCL) in a cohort of 3546 women prospectively followed long term after reconstruction with textured breast implants. J Plast Reconstr Aesthet Surg. 2020;73:841–846.
8. Gidengil CA, Predmore Z, Matkoe S, van Busum K, Kim B. Breast implant-associated anaplastic large cell lymphoma: A systematic review. Plast Reconstr Surg. 2015;135:713–720.
9. National Cancer Center Network. T-cell lymphoma guidelines. Available at: https://www.ncn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed January 20, 2021.
10. McCarthy CM, Loyo-Berríos N, Qureshi AA, et al. Patient Registry and Outcomes for Breast Implants and Anaplastic Large Cell Lymphoma Etiology and Epidemiology (PROFILE): Initial report of findings, 2012–2018. Plast Reconstr Surg. 2019;143:38A. Review of Breast Implant-Associated Anaplastic Large Cell Lymphoma:658–738.
11. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA statement. PLoS Med. 2009;6:e1000097.
12. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: A proposal for reporting: Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. JAMA. 2000;283:2008–2012.
13. Clemens MW, Horwitz SM. NCCN consensus guidelines for the diagnosis and management of breast implant-associated anaplastic large cell lymphoma. Aesthet Surg J. 2017;37:285–289.
14. American Association of Plastic Surgeons. 2019 Plastic surgery statistics. Available at: https://www.plasticsurgery.org/news/plastic-surgery-statistics/sub=2019-Plastic-Surgery-St-attistics. Accessed January 20, 2021.
15. Corrones CJ, Selber JC, Offodile AC. 2nd, Butler CE, Clemens MW. US FDA breast implant postapproval studies: Long-term outcomes in 99,993 patients. Ann Surg. 2019;209:30–36.
16. Doren EL, Miranda RN, Selber JC, et al. U.S. epidemiology of breast implant-associated anaplastic large cell lymphoma. Plast Reconstr Surg. 2017;139:1042–1050.
17. de Boer M, van Leeuwen FE, Hauptmann M, et al. Breast implants and the risk of anaplastic large-cell lymphoma in the breast. JAMA Oncol. 2018;4:335–341.
18. Magnusson M, Beath K, Cooter R, et al. The epidemiology of breast implant-associated anaplastic large cell lymphoma in Australia and New Zealand confirms the highest risk for grade 4 surface breast implants. Plast Reconstr Surg. 2019;143:1285–1292.
19. Tandon VJ, DeLong MR, Ballard TN, et al. Evolving trends in textured implant use for cosmetic augmentation in the United States. Plast Reconstr Surg. 2018;142:1456–1461.
20. Swanson E. Plastic surgeons defend textured breast implants at 2019 U.S. Food and Drug Administration hearing: Why it is time to reconsider. Plast Reconstr Surg Glob Open. 2019;7:e2410.
21. Swanson E. Hall-Findlay E. Banning textured implants is a rational decision to eliminate the risk of breast implant-associated anaplastic large-cell lymphoma (BIA-ALCL). Aesthet Surg J. 2020;40:NP474–NP477.
22. U.S. Food and Drug Administration. Statement from FDA principal deputy commissioner Amy Abernethy, M.D., Ph.D., and Jeff Shuren, M.D., J.D., director of the FDA’s Center for Devices and Radiological Health on FDA’s new efforts to protect women’s health and help to ensure the safety of breast implants. Published March 24, 2020. Available at: https://www.fda.gov/news-events/press-announcements/statement-fda-principal-deputy-commissioner-amy-abernethy-md-phd-and-jeff-shuren-md-jd-director-fdas. Accessed January 24, 2021.
23. Clemens MW, Brody GS, Mahabir RC, Miranda RN. How to diagnose and treat breast implant-associated anaplastic large cell lymphoma. Plast Reconstr Surg. 2018;141:586e–599e.
24. Clemens MW, Medeiros IJ, Butler CE, et al. Complete surgical excision is essential for the management of patients with breast implant-associated anaplastic large-cell lymphoma. J Clin Oncol. 2016;34:160–168.
25. Campanale A, Spagnoli A, Lispi L, Baldorini R, Marletta L. The crucial role of surgical treatment in BIA-ALCL prognosis in early- and advanced-stage patients. Plast Reconstr Surg. 2020;146:530e–538e.
26. Tevis SE, Hunt KK, Miranda RN, et al. Breast implant-associated anaplastic large cell lymphoma: A prospective series of 52 patients. Ann Surg. 2022;40:NP475–NP479.
27. Savage KJ. Prognosis and primary therapy in peripheral T-cell lymphomas. Hematology 2008;1:280–288.
28. Vakilas C, Forero-Torres A. Safety and efficacy of brentuximab vedotin in patients with Hodgkin lymphoma or systemic anaplastic large cell lymphoma. Ther Adv Hematol. 2012;3:209–225.
29. Richardson K, Alrifai T, Grant-Szymanski K, et al. Breast implant-associated anaplastic large-cell lymphoma and the role of brentuximab vedotin (SGN-35) therapy: A case report and review of the literature. Mol Clin Oncol. 2017;6:539–542.
30. Stack A, Levy I. Brentuximab vedotin as monotherapy for unresectable breast implant-associated anaplastic large cell lymphoma. Clin Case Rep. 2019;7:e2410–e2419.
31. Alderuccio JP, Desai A, Yepes MM, Chapman JR, Vega F, Lossos IS. Frontline brentuximab vedotin in breast implant-associated anaplastic large-cell lymphoma. Clin Case Rep. 2018;6:634–637.