Ann Surg Oncol
https://doi.org/10.1245/s10434-025-18598-7

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – BREAST ONCOLOGY

Clinical Features, Microbial Epidemiology, and Recurrence Risk of Cellulitis in Breast Cancer-Related Lymphedema

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ABSTRACT

Background. Cellulitis, resulting from impaired lymphatic function, is a debilitating complication of breast cancer-related lymphedema (BCRL) that contributes to lymphedema progression. However, the clinical presentation and microbiologic profile of BCRL-associated cellulitis remain poorly defined. This study investigated the prevalence, clinical features, and treatment outcomes of cellulitis in BCRL, aiming to identify risk factors for recurrence and inform evidence-based treatment strategies.

Methods. A retrospective review was conducted of cellulitis episodes among 2920 patients with BCRL treated at a single institution between 2000 and 2024. Demographic, clinical, microbiologic, and treatment data were analyzed. Univariate and multivariable Cox proportional hazards models were used to evaluate risk factors associated with recurrent cellulitis.

Results. A total of 418 cellulitis episodes were documented among 231 patients with BCRL, indicating a prevalence of 7.9% (231/2920) and a recurrence rate of 39.0% (90/231). Blood cultures were obtained in 255 (61.7%) episodes, of which 33 (12.9%) were positive. *Streptococcus agalactiae* was the most frequently isolated pathogen (8/33; 24.2%). Risk factors independently associated with recurrence included any radiotherapy (hazard ratio [HR] 2.15; 95% confidence interval [CI] 1.24–3.72; $P < 0.01$), axillary lymph node dissection (HR 1.96; 95% CI 1.05–3.68; $P < 0.05$), and shorter time from BCRL diagnosis to the initial cellulitis episode (HR 0.99; 95% CI 0.99–0.99; $P < 0.01$).

Conclusions. Cellulitis is a significant complication of BCRL with a high recurrence rate. Radiotherapy, axillary lymph node dissection, and early cellulitis onset are associated with recurrence. These findings support proactive surveillance and risk-stratified prevention strategies to reduce infection burden and improve outcomes in this high-risk population.

Keywords Breast cancer · Lymphedema · Lymphatic dysfunction · Cellulitis · Recurrent infection

Cellulitis is among the most challenging complications for patients with breast cancer-related lymphedema (BCRL). As many as 40% of patients with lymphedema experience recurrent cellulitis or lymphangitis, often necessitating antibiotic therapy and hospitalization.[1] This heightened susceptibility significantly decreases patient quality of life and is a drain on healthcare resources.[2–4] Compared with patients with breast cancer without lymphedema, those with BCRL are at more than twice the risk of developing cellulitis, emphasizing the critical interplay between compromised lymphatic function and recurrent bacterial infections.[5,6]

The pathophysiology of cellulitis in patients with lymphedema is distinct from that in individuals without lymphatic impairment. Lymphedema creates a protein-rich environment in stagnant lymphatic fluid, providing an ideal medium for microbial growth.[7–9] Episodes of cellulitis

First Received: 25 July 2025
Accepted: 8 October 2025

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Published online: 19 October 2025

exacerbate lymphatic damage, creating a self-perpetuating cycle of inflammation and lymphedema progression.[7,10] Non-group A streptococci are presumed to be the primary pathogens; however, microbiological cultures often fail to identify causative agents in over 80% of cases.[8,10,11] Several risk factors have been identified for cellulitis in patients with lymphedema, including elevated body mass index (BMI), longer duration of lymphedema, extensive lymph node dissection, radiation therapy, and comorbid conditions such as diabetes mellitus and smoking.[12–15] Delays in the diagnosis and management of lymphedema further compound the risk of both initial and recurrent cellulitis, underscoring the importance of early intervention and effective treatment strategies.[1,16]

Despite the significant clinical impact of cellulitis in BCRL, gaps remain in understanding of its microbial characteristics, optimal therapeutic approaches, and the role of prophylactic antibiotic strategies in preventing recurrence. Existing literature often combines data from both upper- and lower-extremity cellulitis, limiting BCRL-specific analysis and complicating efforts to standardize management. This study investigates the prevalence, clinical presentation, bacterial epidemiology, and treatment outcomes of cellulitis in BCRL, aiming to identify risk factors for recurrent cellulitis and inform evidence-based treatment strategies.

METHODS

Study Population

The institutional review board at Memorial Sloan Kettering Cancer Center approved this study. A retrospective review was conducted of patients who underwent axillary lymph node dissection (ALND) and/or sentinel lymph node biopsy (SLNB) for breast cancer at Memorial Sloan Kettering Cancer Center and were subsequently diagnosed with BCRL between January 2000 and November 2024. Lymphedema was diagnosed based on clinical evaluation and objective limb measurements during visits with specialists in plastic surgery, breast surgery, or rehabilitation medicine, and identified using International Classification of Disease, ninth and tenth edition (ICD-9 and ICD-10) codes (I97.2, I89.0, I97.210, 456, 457, and 457.1). Episodes of cellulitis and other lymphedema-associated infections were identified by querying ICD-9 and ICD-10 codes (L03.x, L04.x, I89.1, L08.x, 682.x, 683, 686.x, and 457.2), followed by manual chart review to confirm true cases of BCRL-associated cellulitis and to extract detailed infection characteristics and treatment data.

Patients were eligible for inclusion if they were aged ≥18 years, had a clinical diagnosis of BCRL, and experienced at least one episode of cellulitis following lymphedema onset. Patients were excluded if their infection occurred before BCRL diagnosis, was unrelated to lymphedema (e.g., surgical site or implant infections), or was managed exclusively at outside institutions and were missing key clinical data.

Study Variables

Variables collected for analysis encompassed patient demographics, clinical characteristics, and infection-related data. Demographic variables included age at first cellulitis episode, sex, self-reported race, and BMI. Self-reported race was categorized as white or non-white, with Asian, Black/African American, Pacific Islander, and other groups classified as non-white. Clinical variables included smoking status, comorbidities (diabetes mellitus, hypertension, coronary artery disease), penicillin allergy, type of breast surgery (breast-conserving surgery or mastectomy), type of axillary surgery (SLNB or ALND), any radiotherapy, nodal radiotherapy, any chemotherapy, timing of chemotherapy (neoadjuvant and/or adjuvant), and date of BCRL diagnosis. Patients who underwent both SLNB and ALND were exclusively classified within the ALND group.

Infection-related variables included the number of documented cellulitis episodes per patient and episode onset dates. Data were collected to distinguish inpatient versus outpatient cellulitis management. For inpatient cases, variables included length of hospital stay, initial antibiotic regimen, duration of therapy, any modifications to treatment, and complications such as sepsis or intensive care unit admission. Microbiological results from blood and wound swab cultures were recorded when available. For outpatient cases, antibiotic regimen details, including type, duration, and any modifications during treatment, were recorded. Vital signs and laboratory findings, including body temperature and white blood cell count, were collected for both inpatient and outpatient cases when available. For patients who received prophylactic antibiotics, the specific agents were recorded.

To standardize the evaluation of empiric antibiotic therapy, regimens were categorized by antimicrobial spectrum as follows: (a) anti-Gram-positive agents excluding methicillin-resistant *Staphylococcus aureus* (MRSA), penicillin-based (amoxicillin, oxacillin, penicillin, amoxicillin-clavulanate, ampicillin-sulbactam, piperacillin-tazobactam, ticarcillin-clavulanate); (b) anti-Gram-positive agents excluding MRSA, cephalosporin-based (cefazolin, cephalexin, cefadroxil, ceftriaxone, cefuroxime, cefepime); (c) anti-Gram-positive agents with MRSA coverage (vancomycin, trimethoprim-sulfamethoxazole, daptomycin, linezolid, doxycycline, clindamycin); (d) anti-Gram-negative/other agents (aztreonam, ciprofloxacin, levofloxacin, clarithromycin, metronidazole); and (e) combination regimens providing both anti-Gram-positive and anti-Gram-negative coverage.

The primary outcome of this study was recurrence of cellulitis, defined as two or more episodes occurring after the diagnosis of BCRL. The secondary outcome was the prevalence of cellulitis, defined as the proportion of patients with BCRL experienced at least one documented cellulitis episode during the study period. Follow-up duration was calculated from the date of the BCRL diagnosis to the last recorded clinic visit or death, whichever occurred first. Time intervals between multiple episodes of cellulitis were calculated to analyze recurrence patterns.

Statistical Analysis

Patient demographics, infection characteristics, and treatment regimens were summarized by descriptive statistics. Continuous variables were reported as medians with interquartile ranges (IQRs), and categorical variables were presented as counts and proportions. Univariate and multivariable Cox proportional hazard models were used to evaluate risk factors associated with recurrent cellulitis, adjusting for key patient characteristics, with results reported as hazard ratios (HRs) and 95% confidence intervals (CIs). Baseline characteristics included in the model were selected a priori based on clinical relevance and included age at first cellulitis episode, BMI, race (white vs non-white), smoking status, diabetes mellitus, hypertension, coronary artery disease, penicillin allergy, type of axillary surgery (SLNB vs ALND), any chemotherapy, any radiotherapy, nodal radiotherapy, and time interval from BCRL diagnosis to the first episode of cellulitis. Variables selected in the final multivariable Cox regression model were chosen based on clinical and statistical significance. All analyses were performed using SAS software version 9.4 (SAS Institute, Inc.), and a P value <0.05 was considered statistically significant.

RESULTS

Patient and Clinical Characteristics

Among 2920 patients diagnosed with BCRL, 231 (7.9%) experienced at least one episode of BCRL-associated cellulitis and were included in the analysis. Of these, 141 (61.0%) experienced a single episode of cellulitis and 90 (39.0%) had recurrent episodes. All patients were female and predominantly white (80.1%), with a median age of 58 (IQR 49–66) years and a median BMI of 25.2 (IQR 22.5–29.5) kg/m^2. Most patients had undergone ALND (81.0%), mastectomy (71.9%), and radiotherapy (73.2%) as part of their breast cancer treatment. The median follow-up duration from BCRL diagnosis was 85.5 (IQR 42.8–137.6) months, with a median of 72.5 (IQR 38.1–128.9) months for patients without recurrence and 99.4 (IQR 65.4–138.9) months for patients with recurrent cellulitis. Patient demographic and clinical characteristics are summarized in Table 1.

Cellulitis Prevalence, Recurrence Rate, and Clinical Features

A total of 418 cellulitis episodes were documented among 231 patients with BCRL, indicating a cellulitis prevalence of 7.9% (231/2920) and a recurrence rate of 39.0% (90/231). The number of cellulitis episodes per patient ranged from 1 to 12, with a median of 1 (IQR 1–2) episode during the study period. Clinical and laboratory characteristics of the cellulitis episodes stratified by recurrence status are summarized in Table 2. Inpatient admission for intravenous antibiotics was required in 63.2% (261/413) of cases, with a median hospital stay of 3 (IQR 2–4) days. Fever (temperature ≥38 °C) was documented in only 17% of episodes. The median time from lymphedema onset to first cellulitis episode was shorter in recurrent

TABLE 1 Patient and clinical characteristics of the overall study cohort

Characteristic	Overall cohort (n=231)
Age, years	58 (49–66)
Sex	
Female	231 (100)
Male	0 (0)
BMI, kg/m^2	25.2 (22.5–29.6)
Race	
White	185 (80.1)
Non-white	46 (19.9)
Smoking (current or former)	70 (30.3)
Diabetes mellitus	49 (21.2)
Hypertension	125 (54.1)
Coronary artery disease	17 (7.4)
Penicillin allergy	41 (17.7)
Type of axillary surgery	
SLNB only	44 (19.0)
ALND	187 (81.0)
Type of breast surgery	
BCS	65 (28.1)
Mastectomy	166 (71.9)
Any radiotherapy	169 (73.2)
Nodal radiotherapy	64 (27.7)
Any chemotherapy	202 (87.4)
Chemotherapy timing	
Adjuvant	130 (64.4)
Neoadjuvant	72 (35.6)

Data are presented as median (interquartile range) or n (%) unless otherwise indicated

ALND, axillary lymph node dissection; BCS, breast-conserving surgery; BMI, body mass index; SLNB, sentinel lymph node biopsy

TABLE 2 Clinical and laboratory characteristics of cellulitis episodes in patients with breast cancer-related lymphedema (BCRL), stratified by recurrence

Number of cellulitis episodes	Overall ($n=418$)	Nonrecurrent ($n=141$)	Recurrent ($n=277$)
Patients	231 (100)	141 (61.0)	90 (39.0)
Admitted to hospital	262 (62.7)	80 (56.7)	182 (65.7)
Hospital stay, days	3 (2–4)	3 (2–4)	3 (2–4)
Temperature ≥38°C,[a]	68 of 397 (17.1)	18 of 132 (13.6)	50 of 265 (18.9)
WBC >11 K/mcL[b]	84 of 369 (22.8)	13 of 124 (10.5)	71 of 245 (29.0)
Bacteremia[c]	33 of 255 (12.9)	6 of 74 (8.1)	27 of 181 (14.9)
ICU-level care/sepsis	12 (2.9)	3 (2.1)	9 (3.2)
Months from lymphedema onset to first cellulitis episode	9.1 (1.3–37.0)	13.9 (2.9–42.8)	4.9 (0.6–29.1)
Months between cellulitis episodes	–	–	8.4 (2.5–19.7)
Follow-up time, months	85.5 (42.8–137.6)	72.5 (38.1–128.9)	99.4 (65.4–138.9)

Data are presented as median (interquartile range) or *n* (%) unless otherwise indicated

ICU, intensive care unit; WBC, white blood cell count

[a]Includes all episodes in which temperature was collected ($n=397$ of 418)

[b]Includes all episodes in which WBC was collected ($n=369$ of 418)

[c]Includes all episodes in which blood culture was collected ($n=255$ of 418)

cases (4.9 months, IQR 0.6–29.1) compared with nonrecurrent cases (13.9 months, IQR 2.9–42.8). Leukocytosis (white blood cell count >11 k/mcL) was observed in 29.0% of recurrent episodes versus 10.5% of nonrecurrent episodes. Among patients with recurrent infections, the median interval between episodes was 8.4 (IQR 2.5–19.7) months, and the interval appeared to decrease on average with each subsequent infection (Fig. 1).

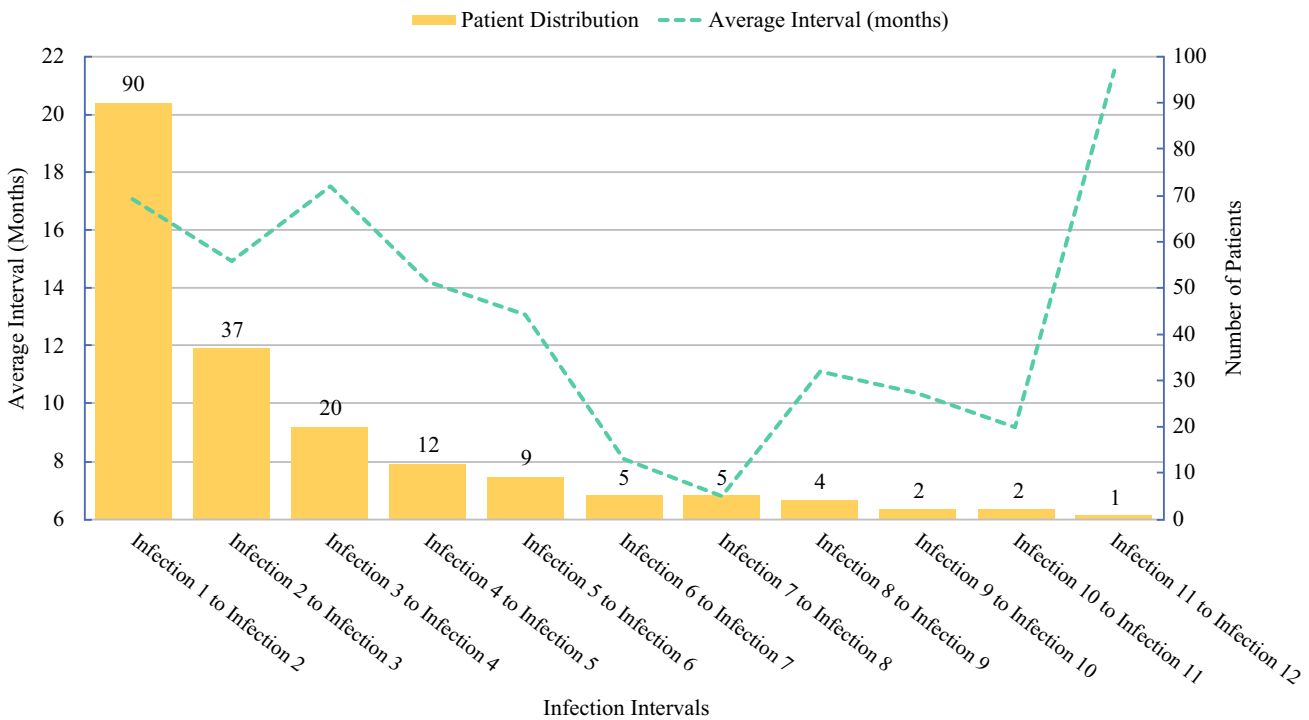

FIG. 1 Interval duration and patient distribution across recurrent cellulitis episodes in breast cancer-related lymphedema (BCRL) ($N=277$ episodes, 90 patients). Bar graph indicates the number of patients experiencing each cellulitis interval, from the first to the 12th episode. The line graph depicts the corresponding average interval in months between each infection. Most patients experienced only one cellulitis episode, with a sharp drop in patient count as the number of infections increased. Average time between infections generally decreased with subsequent episodes, except for a rise at later intervals where sample size was limited

Microbial Epidemiology and Antibiotic Treatment of Cellulitis Episodes

Of 413 documented cellulitis episodes, blood cultures were obtained in 255 (61.7%) cases, with 33 (12.9%) returning positive. *Streptococcus agalactiae* was the most frequently isolated pathogen, identified in 8 of the 33 positive blood cultures (24.2%). Wound swab cultures were collected in 21 episodes involving skin breakdown, with 10 (47.6%) yielding positive results. Table 3 summarizes all bacterial species isolated from positive blood and wound swab cultures obtained during cellulitis episodes. The initial empiric antibiotic regimen was effective without modification in 87.4% (354/405) of episodes. The most common first-line antibiotics were cephalosporin-based agents targeting Gram-positive bacteria, excluding MRSA (59.5%), followed by agents with MRSA coverage (26.2%). Among patients receiving prophylactic antibiotics, 58.6% (17/29) remained infection free throughout the duration of follow-up.

Predictors of Recurrent Cellulitis in BCRL

In multivariable Cox regression analysis (Table 4), any radiotherapy (HR 2.15; 95% CI 1.24–3.72; $P < 0.01$), ALND (HR 1.96; 95% CI 1.05–3.68; $P < 0.05$), and shorter time from lymphedema onset to initial infection (HR 0.99; 95% CI 0.99–0.99; $P < 0.01$) were significantly associated with an increased risk of recurrent cellulitis. Age, BMI, smoking status, penicillin allergy, coronary artery disease, and race were insignificantly associated with the risk of recurrent cellulitis.

TABLE 3 Microbiological characteristics of cellulitis episodes in patients with breast cancer-related lymphedema (BCRL)

Bacteria isolated from positive blood cultures (n=33)	*N*
Streptococcus agalactiae	8
Streptococcus mitis	6
MSSA	6
Coagulase-negative staphylococcus	3
Streptococcus dysgalactiae group	2
Streptococcus viridans group	2
Streptococcus gordonii	1
Beta hemolytic streptococcus group b	1
S. mitis + *Streptococcus pneumoniae*	1
Staphylococcus lugdunensis	1
S. pneumoniae	1
Streptococcus oralis	1
Bacteria isolated from positive wound cultures (n=10)	
MSSA	5
S. lugdunensis + Coagulase-negative staphylococcus	2
MRSA	1
Coagulase-negative staphylococcus	1
Pseudomonas aeruginosa + *Staphylococcus mitis*	1

MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.

TABLE 4 Multivariable cox proportional hazards regression model for risk factors associated with recurrent cellulitis in breast cancer-related lymphedema (BCRL)

Characteristic	HR	95% CI	*P* value
Age, per 1 year increase	1.00	0.98–1.02	0.78
BMI, per 1 kg/m^2 increase	1.00	0.96–1.05	0.78
Race			
White	–	–	
Non-white	0.55	0.29–1.01	0.06
Smoking (current or former)	0.98	0.62–1.55	1.55
Coronary artery disease	1.29	0.61–2.72	0.51
Penicillin allergy	1.33	0.78–2.28	0.29
Type of axillary surgery			
SLNB only	–	–	
ALND	1.96	1.05–3.68	<0.05*
Any radiotherapy	2.15	1.24–3.72	<0.01*
Time from BCRL diagnosis to first infection, per 1 month increase	0.99	0.99–0.99	<0.01*

ALND, axillary lymph node dissection; BMI, body mass index; CI, confidence interval; HR, hazard ratio; SLNB, sentinel lymph node biopsy

*Statistically significant values

DISCUSSION

In this retrospective cohort study of patients with BCRL treated at a single tertiary cancer center, 7.9% developed at least one episode of cellulitis, and over one-third of these patients experienced recurrent infections. To the best of our knowledge, this is the first study to provide an in-depth, large-scale analysis of the clinical characteristics, microbiology, and recurrence risk of cellulitis specifically among patients with BCRL. Drawing on more than two decades of institutional experience at a high-volume center specializing in lymphedema management, these findings provide novel insights into this distinct patient population.

The cellulitis prevalence (7.9%) and recurrence rate (39.0%) observed in this cohort were notably lower than figures previously reported in the literature, where recurrence rates have reached as high as 56.6%.[17,18] This discrepancy may be explained by differences in study populations. Previous epidemiological reports by Park et al.[17] and Rodriguez et al.[18] included patients with both upper- and predominantly lower-extremity lymphedema, the latter of which is known to carry a higher risk of recurrence because of the greater bacterial burden and more pronounced lymphatic stasis.[9,19,20] By contrast, the present study focused exclusively

on patients with upper-extremity lymphedema secondary to breast cancer, which may account for the lower rates.

Despite the significant clinical burden, microbiologic confirmation of causative organisms in this study was limited. Blood cultures were obtained in only 62% of episodes, yielding a positivity rate of 12.9%. *S. agalactiae* was the most frequently isolated pathogen, consistent with prior research indicating a predominance of non-group A streptococci in lymphedema-associated cellulitis.[10,17,18] In contrast, cellulitis in non-lymphedema populations is more commonly associated with *Streptococcus pyogenes* and *S. aureus*, albeit with similarly low bacteremia rates.[21–23] Notably, the positive blood culture rate observed among our cohort of patients with BCRL (12.9%) was higher than typically reported in community-acquired cellulitis, possibly because of the compromised bacterial filtration in lymphedematous tissue facilitating earlier systemic dissemination.[8,10]

Empiric therapy targeting Gram-positive organisms without MRSA coverage was effective in most cases. Cephalosporin-based regimens demonstrated high efficacy, and modification or escalation of antibiotic therapy was infrequently required. These findings support current empiric treatment guidelines and suggest that broad-spectrum coverage targeting MRSA may not be necessary in most cases of BCRL-associated cellulitis.[24–26] Prophylactic antibiotics appeared beneficial in selected patients, with more than half remaining infection-free during follow-up. Although the small sample size precludes definitive conclusions, these results are consistent with existing recommendations for prophylaxis with cephalosporin-based regimens or penicillin in high-risk individuals to prevent recurrent cellulitis.[24] In patients with BCRL, one study found that biweekly intramuscular benzathine penicillin (2.4 MU) reduced the frequency of recurrent cellulitis episodes, but it lacked a control group.[27] Randomized trials and meta-analyses in mixed populations evaluating antibiotic prophylaxis for recurrent cellulitis demonstrate a clear benefit during active therapy, but protection wanes after discontinuation.[28,29] Adverse effects are typically mild but may include allergy, drug reactions, and *Clostridioides difficile* infection.[21,28] Notably, none of the major trials or systematic reviews in cellulitis have systematically assessed the development of antimicrobial resistance during prophylaxis, though evidence from other settings (e.g., urinary tract infections) raises concern about the potential for resistance with long-term or repeated courses.[30,31] Thus, clinicians must balance potential benefits against these risks, reserving prophylaxis for carefully selected high-risk patients with close monitoring.

Radiotherapy and ALND emerged as significant predictors of recurrent cellulitis. This finding aligns with the understood pathophysiology of lymphedema, in which these interventions disrupt lymphatic drainage and impair local immune responses, thereby enhancing susceptibility to infection.[32,33] Additionally, radiation-induced lymphatic injury and epithelial dysfunction may contribute to increased susceptibility to recurrent infection, compounding the risk in this population.[34–36] A shorter interval between BCRL onset and the initial cellulitis episode was also significantly associated with increased recurrence risk, and subsequent episodes tended to occur at progressively shorter intervals. This pattern likely reflects the progressive nature of lymphedema-associated cellulitis, characterized by a vicious cycle of inflammation, infection, and worsening lymphatic dysfunction.[7,10,37,38]

Emerging data highlight the role of skin barrier dysfunction and microbiome alterations in the pathogenesis of cellulitis in BCRL. Recent studies using both human and mouse models have demonstrated that lymphedema impairs epidermal integrity and tight junction function, which may directly facilitate bacterial entry and increase infection risk.[39] In parallel, alterations in the skin microbiome—including decreased diversity and increased colonization with pathogenic bacteria—have also been implicated in the pathophysiology of cellulitis among patients with lymphedema.[40] These mechanisms may underlie the high recurrence rate observed in this cohort and underscore the multifactorial nature of susceptibility in BCRL.

These findings underscore the need for clinicians to prioritize early and proactive management strategies for BCRL-associated cellulitis, particularly in patients receiving radiotherapy or ALND, or those presenting with rapid-onset cellulitis following BCRL diagnosis. In addition to managing underlying risk factors, providers should consider individualized lymphedema therapy plans, prophylactic antibiotic regimens, and timely referral for microsurgical interventions, such as lymphovenous bypass or vascularized lymph node transplant, which have demonstrated promising reductions of recurrent cellulitis and improved patient outcomes compared with conservative measures such as complete decongestive therapy.[41–44] Although blood cultures often have low diagnostic yield, obtaining them in patients who are sufficiently ill to require hospitalization for a cellulitis episode may aid in guiding targeted antimicrobial therapy and enhancing understanding of microbial epidemiology. Future research should focus on prospective evaluations of prophylactic antibiotic strategies and microsurgical techniques to determine their long-term effectiveness in reducing cellulitis recurrence and improving patient-reported outcomes. Additionally, studies incorporating objective limb volume measurements and advanced imaging modalities, such as lymphoscintigraphy, may help clarify the relationship between lymphedema severity and cellulitis risk.

Study Limitations

This study has several limitations. As a retrospective single-institution analysis, the potential for selection bias may limit the generalizability of our findings. Lymphedema diagnosis was based on ICD codes, and data on lymphedema severity, such as limb volume measurements or bioimpedance spectroscopy (L-Dex) scores, were unavailable. As a result, the relationship between cellulitis risk and lymphedema severity could not be fully explored, and no imaging studies (e.g., lymphoscintigraphy) were used to further characterize lymphatic dysfunction. However, the use of ICD coding was deemed the most practical approach given the retrospective design and the lack of consensus around diagnostic criteria for lymphedema.[45–47]

Additionally, cellulitis episodes may have been underreported, as patients could have sought care at external facilities rather than return to our institution, potentially leading to an underestimation of infection prevalence and recurrence. In some cases, cellulitis and lymphedema were diagnosed concurrently, complicating efforts to determine whether lymphedema served as a predisposing factor or developed secondary to infection, underscoring the complex, bidirectional relationship between cellulitis and secondary lymphedema. To minimize this potential source of bias, patients with concurrent diagnoses were excluded from the analysis.

Finally, the modest sample size may have limited statistical power and increased the risk of type I error. However, to the best of our knowledge, this represents the largest retrospective cohort study to date examining cellulitis recurrence in patients with BCRL. Larger, prospective studies are warranted to validate and expand upon these findings.

CONCLUSIONS

Cellulitis remains a significant and recurrent complication in patients with BCRL, with a prevalence of 7.9% and a recurrence rate of 39.0% identified in this large single-institution cohort. Radiotherapy, ALND, and shorter time from lymphedema diagnosis to initial infection emerged as key risk factors for recurrence, highlighting the heightened vulnerability of these patients to repeated infections. The observation that early-onset cellulitis was strongly associated with recurrence and that subsequent infections occurred at progressively shorter intervals underscores the importance of vigilant monitoring and timely intervention in patients with BCRL who develop cellulitis. Although microbiologic confirmation was infrequent, *Streptococcus* species predominated in cases of bacteremia, and empiric cephalosporin-based regimens proved effective in most cases. These findings point to the need for prospective studies evaluating prophylactic antibiotic strategies and surgical interventions to better define effective approaches for reducing cellulitis recurrence and improving long-term outcomes.

ACKNOWLEDGMENTS This research was supported in part by the National Institutes of Health through grants R01HL111130, R01CA278599, R21AR081076, and R21AG076132 awarded to Dr. Mehrara; R21AG077150 awarded to Dr. Kataru; and the Cancer Center Support Grant P30CA008748 that supports the research infrastructure at Memorial Sloan Kettering Cancer Center.

DISCLOSURE Dr. Mehrara has received investigator-initiated grants from Pfizer, Regeneron, Atyr, and Integra; royalties from PureTech and Elsevier; and serves as a consultant for Mediflix Corp. Dr. Barrio has received speaking honoraria from MSD and Novartis. The other authors have no disclosures to report.

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