The rate of breast cancer surgery has increased through the years, mainly due to the use of improved methods of cancer detection, such as radiological and genetic testing. Simultaneously, due to improved favorable economic factors, improvements in implant design, and the widespread successful use of acellular dermal matrix (ADM), breast reconstruction with tissue expanders (TEs) and implants is becoming increasingly popular among patients who have undergone mastectomy due to breast cancer prevention or treatment.1,2 The American Society of Plastic Surgeons reported that, in 2017, its members performed approximately 106,000 breast reconstructive procedures in the United States alone.3 Of these patients, approximately 74,000 underwent breast reconstruction with TEs and implants, whereas the remaining patients had autologous reconstructions.

Unfortunately, the rate of infection after breast implant reconstruction, which varies by hospital and region, rever...
mains unacceptably high, ranging from 2.5% to 24%.4–6 Infections that do not respond to antibiotic treatment alone usually require further surgery and explantation of the device, which is devastating for both patients and physicians.

Randomized controlled studies have demonstrated that prophylactic antibiotics are effective in preventing surgical wound infections.7 However, the most frequently utilized perioperative antimicrobials, mainly first-generation cephalosporins, do not cover commonly encountered skin pathogens, such as methicillin-resistant Staphylococcus aureus (MRSA) and coagulase-negative Staphylococcus resistant to methicillin (CNS-R), which are responsible for over two-thirds of all breast implant-related infections.8 The baseline skin and axillary microbial flora that are contiguous with the surgical incision site and the axillary surgical drains, which usually remain in place for 1–2 weeks, are the pathogens most likely to cause a surgical site infection (SSI).9 Therefore, selecting targeted, prophylactic perioperative antimicrobials on the basis of patients’ baseline microbial skin flora, instead of following a standard empirical “one size fits all” approach, seems a reasonable means of reducing SSIs. Several studies have demonstrated that the use of targeted perioperative antimicrobials, concordant with patients’ baseline microbial flora, has been associated with a decrease in postoperative SSI.10,11 We conducted this prospective observational study of patients undergoing postmastectomy implant-based reconstructive procedures to determine whether the use of antimicrobial prophylaxis concordant with patients’ baseline axillary microbial flora reduces the risk of postsurgical site infections.  

**METHODS**

**Patient Population**

We prospectively enrolled 241 patients who were scheduled for a postmastectomy, 2-stage, implant-based breast reconstruction at our institution between September 2015 and January 2018. For all patients, baseline axillary swab (eSwab; Copan Diagnostics Inc., Murrieta, CA) cultures were obtained from the ipsilateral surgical site within 2 weeks before surgery, and every aerobic and anaerobic bacterial species recovered was identified. The surgeons who prescribed the patients’ perioperative antimicrobials were blinded to the results of the swab test. All patients were followed up for at least 6 months postoperatively and evaluated for potential surgical complications, including SSIs. Our study was approved by The University of Texas MD Anderson Cancer Center’s Institutional Review Board. Written informed consent was obtained from all participants.

**Data Collection and Definitions**

We prospectively gathered information on patients’ demographics, baseline comorbidities, breast cancer characteristics, cancer treatments, timing of TE placement, operative approaches, axillary drain tube durations, and postoperative complications. We also recorded the use of all perioperative antimicrobials—including systemic perioperative, subpectoral pocket irrigation, and postoperative oral antimicrobials—and confirmed all of them via electronic chart reviews plus inpatient and outpatient pharmacy records. The use of perioperative antimicrobials was defined as concordant if the baseline axillary flora were susceptible to the antibiotic the patient received and discordant if they were not. We also identified all patients who developed an SSI, as defined by the Centers for Disease Control and Prevention.12

**Microbiology**

Once a patient’s axilla was swabbed, the specimen was submitted on the same day to the microbiology department for further processing. These specimens were inoculated onto solid media for aerobic and anaerobic culture. The aerobic culture media consisted of chocolate II agar (Gonococcus [GC] II Agar with hemoglobin and IsoVitalex; BD, Franklin Lakes, NJ; catalog 221267), trypticase soy agar with 5% sheep blood (BD; catalog 221261), MacConkey II agar (BD; catalog 221270), and Columbia Naladixic Acid (CNA) agar with 5% sheep blood (BD; catalog 221353). After inoculation, the aerobic culture was incubated at 35°C for 48 hours and observed for colony growth. Colonies growing on the culture were identified phenotypically to the genus and/or species level. The anaerobic culture consisted of preduced media purchased from Anaerobe Systems (Morgan Hill, CA; catalog AS-303): Brucella agar, laked blood kanamycin-vancomycin agar, and phenylethyl alcohol agar. After inoculation, the anaerobic culture was incubated at 35°C in anaerobic conditions using the Anoxomat System (Advanced Instruments, Norwood, MA) with an atmosphere of 5% hydrogen, 10% carbon dioxide, and the balance of nitrogen. Cultures were held for 7 days and observed for colony growth. Colonies growing on the culture were identified phenotypically to the genus and/or species level. All isolated Staphylococcus species were tested for susceptibility to oxacillin, clindamycin, trimethoprim/sulfamethoxazole, and tetracycline using ETEST strips (bioMérieux, Inc., Durham, NC). All isolated Gram-negative bacilli were tested for susceptibility testing performed on the Vitek2 AST instrumentation (bioMérieux, Inc.) using the XN06 and GN09 cards (bioMérieux, Inc.).

**Statistical Analysis**

Categorical variables were compared using the Chi-square or Fisher’s exact test, as appropriate. Continuous variables were compared using the Wilcoxon rank-sum test. Kaplan-Meier method was used to estimate the cumulative incidence curves of infection, and log-rank test was used for curve comparison. All tests were 2-sided tests with a P value <0.05 considered statistically significant. The data analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, NC).

**RESULTS**

**Clinical Characteristics**

A total of 241 patients had a postmastectomy, implant-based breast reconstruction. Of these, 33 patients (14%) developed an SSI (Table 1). The mean age of the patients
who developed a postoperative infection (53 years; range, 32–76 years) was higher than that of uninfected patients (47 years; range, 22–81 years; \( P = 0.01 \)). A larger bra cup size (D to E) was also a risk factor for infection compared with smaller breast cup sizes (A to C) \( (P = 0.0003) \). Similarly, patients with a larger body mass index (median, 27.3; interquartile range [IQR], 23.3–31.6) were more likely to develop an SSI than were those with a smaller body mass index (median, 25.9; IQR, 22.6–30.5), although the difference was not significant \( (P = 0.19) \). Additionally, the development of a postoperative seroma or hematoma, which is usually associated with having a postsurgical drain for an extended duration \( (P = 0.002) \), was also associated with a higher risk of infection \( (P < 0.0001) \). The presence of skin flap necrosis \( (P = 0.09) \) and use of ADM \( (P = 0.12) \) were more common in patients with a postoperative infection but did not reach statistical significance. Furthermore, hypertension; diabetes; the use of tobacco or alcohol; the type of tumor or extension; the use of chemotherapy, radiotherapy, or hormonal therapy; and the timing of surgery were not risk factors for infection \( (P > 0.07 \text{ for each}) \).

### Baseline Axillary Microbial Flora

Axillary fossa swabs showed that 151 patients (63%) had polymicrobial flora, 59 (24%) had monomicrobial flora, and 31 (13%) had no positive culture. None of these results were associated with a greater risk of infection \( (P = 0.09, P = 0.18, \text{ and } P = 0.78, \text{ respectively}) \) (Table 2). Additionally, neither aerobic (Gram positive and Gram negative) nor anaerobic organisms were more common in patients who developed an infection than in those who did not \( (P \geq 0.14 \text{ for all}) \). This was also true if the organisms were grouped as CNS, regardless of resistance to methicillin \( (P = 0.90) \); *Staphylococcus aureus* \( (P > 0.99) \); *Streptococcus pyogenes* \( (P > 0.99) \); *Enterococcus faecalis* \( (P > 0.99) \); *Enterococcus faecium* \( (P > 0.99) \); and *Micrococcus luteus* \( (P > 0.99) \).
or any *Staphylococcus* species (CNS and *S. aureus*), with ($P = 0.84$) or without ($P = 0.74$) resistance to methicillin.

### Prophylactic Antimicrobial Regimens

All patients received standardized perioperative systemic antimicrobial therapy (Table 3). The most common drugs used were cefazolin (215 patients; 89%), clindamycin (20 patients; 8%), and vancomycin (6 patients; 3%). Thereafter, at the discretion of each surgeon, all patients received subpectoral pocket irrigation with a broad-spectrum antimicrobial solution. The most commonly used regimen was bacitracin plus polymyxin B (44%), followed by bacitracin, cefazolin plus gentamicin (38%) and bacitracin, polymyxin B plus gentamicin (11%). After surgery, oral prophylactic antibiotics were used in 99% of cases, either for a week or until the drainage catheters were removed. The most commonly prescribed postsurgical antimicrobial drugs were cefadroxil (61%), trimethoprim/sulfamethoxazole (15%), and clindamycin (10%). None of the antimicrobials utilized were statistically associated with a higher rate for postsurgical site infections ($P > 0.23$).

### Concordance Between Prophylactic Antimicrobials and Baseline Axillary *Staphylococci* Flora

A total of 31 patients (13%) did not have any bacterial growth upon baseline axillary cultures, and 11 patients (5%) did not have any *Staphylococci* growth, for which these patients were not utilized in this part of the analysis (Table 4). Only 108 patients (54%) received a concordant systemic perioperative antimicrobial, whereas 107 patients (54%) received a concordant postoperative oral antimicrobial. In other words, in both the perioperative and the postoperative periods, approximately half of the patients received an antimicrobial to which the baseline axillary *Staphylococci* flora were resistant. Moreover, the probability that the combination of both peri- and postoperative antimicrobials was discordant was 40%. However, whether the patient received a concordant or discordant antimicrobial combination did not predict for infection ($P \geq 0.72$; Fig. 1).

### Concordance Between Prophylactic Antimicrobials and Baseline Gram-Negative Axillary Flora

A total of 7 patients (3%) had Gram-negative rods on their baseline preoperative axillary cultures (Table 2). Although all patients received discordant antimicrobials (6 patients received perioperative cefazolin followed by postoperative cefadroxil, and 1 patient received perioperative and postoperative clindamycin), only 1 patient developed an infection. In this individual, no cultures were done at the time of infection owing to the lack of any abnormal drainage; however, the implant was successfully salvaged with use of our standardized red breast

### Table 2. Baseline Axillary Microbial Flora

| Variable                                      | Noninfected Patients (n = 208) n (%) | Infected Patients (n = 33) n (%) | P    |
|-----------------------------------------------|-------------------------------------|--------------------------------|------|
| Presence and type of organisms                |                                     |                                 |      |
| Culture negative                              | 28 (13)                             | 3 (9)                           | 0.78 |
| Monomicrobial                                 | 54 (26)                             | 5 (15)                          | 0.18 |
| Polymicrobial                                 | 126 (61)                            | 25 (76)                         | 0.09 |
| Single organisms*                             |                                     |                                 |      |
| Aerobic Gram-positive organisms               | 172 (83)                            | 29 (88)                         | 0.46 |
| CNS-S                                         | 139 (67)                            | 23 (70)                         | 0.74 |
| CNS-R                                         | 73 (35)                             | 11 (33)                         | 0.84 |
| MSSA                                          | 2 (1)                               | 0 (0)                           | >0.99|
| MRSA                                          | 0                                   | 0                               | >0.99|
| Micrococcus spp.                              | 15 (7)                              | 2 (6)                           | >0.99|
| Stomatococcus spp.                            | 2 (1)                               | 0 (0)                           | >0.99|
| Streptococcus, alpha hemolytic                | 5 (2)                               | 0 (0)                           | >0.99|
| Lactobacillus spp.                            | 1 (0.5)                             | 1 (3)                           | 0.26 |
| Corynebacterium spp.                          | 21 (10)                             | 6 (18)                          | 0.23 |
| Bacillus spp.                                 | 22 (11)                             | 5 (15)                          | 0.39 |
| Dermabacter spp.                              | 1 (0.5)                             | 0 (0)                           | >0.99|
| Aerobic Gram-negative organisms               | 6 (3)                               | 1 (3)                           | >0.99|
| Enterobacter spp.                             | 1 (0.5)                             | 1 (3)                           | 0.26 |
| Neustrophomonas spp.                          | 0 (0)                               | 1 (3)                           | 0.14 |
| Sphingomonas spp.                             | 1 (0.5)                             | 0 (0)                           | >0.99|
| Pseudomonas spp.                              | 2 (1)                               | 0 (0)                           | >0.99|
| Acinetobacter spp.                            | 2 (1)                               | 0 (0)                           | >0.99|
| Anaerobic organisms                           | 72 (35)                             | 11 (33)                         | 0.89 |
| Peptostreptococcus spp.                       | 66 (32)                             | 11 (33)                         | 0.89 |
| Prevotella spp.                                | 1 (0.5)                             | 0 (0)                           | >0.99|
| Clostridium spp.                              | 2 (1)                               | 0 (0)                           | >0.99|
| Combined organisms*                           |                                     |                                 |      |
| All CNS (CNS-S and CNS-R)                     | 172 (83)                            | 27 (82)                         | 0.90 |
| All SA (MSSA and MRSA)                        | 2 (1)                               | 0 (0)                           | >0.99|
| All methicillin-sensitive *Staphylococci* (CNS-S and MSSA) | 139 (67)                            | 23 (70)                         | 0.74 |
| All methicillin-resistant *Staphylococci* (CNS-R and MRSA) | 73 (35)                             | 11 (33)                         | 0.84 |

*If two of the same organisms were encountered in the same patient, it was counted once.

CNS-R, coagulase-negative *Staphylococci* resistant to methicillin; CNS-S, coagulase-negative *Staphylococci* sensitive to methicillin; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; SA, *Staphylococcus aureus*; spp, species.
protocol, which utilizes empiric ciprofloxacin, doxycycline, and rifampin.

Surgical Site Infections

A total of 33 patients (14%) developed an SSI, of whom 15 (45%) eventually needed TE explantation because of lack of response to antimicrobial treatment or advanced stage of infection. The median time from initial surgery to infection was 35 days (IQR, 21–95 days). Twelve (36%) of the patients with an SSI had an axillary drain in place at the onset of infection.

Of the 33 patients who developed a postoperative infection, 8 patients (24%) did not have any cultures performed owing to the lack of drainage or surgery (100% of implants were salvaged); 7 patients (21%) had cultures done, but with negative bacterial growth (71% of implants were salvaged); and 18 patients (55%) had cultures that showed positive microbial growth (28% of implants were salvaged). Of the latter group of 18 patients, only 5 (28%) had postoperative cultures which grew the same pathogen as that seen in the patient’s baseline axillary cultures (CNS-R in all cases). Two of these patients had received concordant perioperative and postoperative antimicrobials, 2 had received 1 concordant antimicrobial, and 1 patient had received both discordant antimicrobials. The remaining 13 patients (72%) had a different pathogen than that seen in the baseline axillary culture. Five of these patients had Gram-positive organisms (CNS-R, MRSA, Corynebacterium, and Bacillus species, 1 patient each); 6 patients had Gram-negative organisms (Serratia marcescens and Pseudomonas species, 3 patients each); 1 patient had a Mycobacterium abscess; and 1 patient had a mixed infection with CNS-R plus Pseudomonas.

DISCUSSION

Our study reveals that the use of concordant or discordant systemic perioperative and/or postoperative oral antimicrobial prophylaxis targeting the most common organisms colonizing the axillary flora, specifically Staphylococci species, did not reflect in a statistically significant decrease or increase in SSIs. However, because approximately half of the patients received discordant antimicrobials and did not develop an SSI, it is possible that (a) the baseline axillary flora are not risk factors for infection, (b) modern sterile surgical techniques plus intraoperative broad-spectrum antimicrobial pocket irrigations are adequate for preventing SSIs, or (c) the multiple risk factors for infection, as discussed below, may have confounded our findings for which a larger sample size would be needed to observe a statistically significant difference.

Patients undergoing implant-based reconstruction have several intrinsic risk factors that place them at a higher risk for infection than patients undergoing nonreconstructive breast surgeries. Our study, like others, identified that older age, greater body mass index, larger breast cup size, longer duration of axillary surgical drains, and development of a postsurgical seroma and/or hematoma were all associated with a higher risk for infection. Furthermore, we identified a trend toward developing SSIs among patients who developed a postsurgical skin flap necrosis or in whom ADMs were used. However, we did not observe a statistically significant correlation between SSIs and other risk factors identified in the literature, such as

Table 3. Perioperative and Postoperative Prophylactic Antimicrobial Regimens

| Antimicrobial Regimens                  | Noninfected Patients (n = 208) n (%) | Infected Patients (n=33) n (%) | P       |
|-----------------------------------------|-------------------------------------|--------------------------------|---------|
| Perioperative systemic antimicrobials    |                                     |                                |         |
| Cefazolin                               | 184 (88)                            | 31 (94)                        | 0.55    |
| Clindamycin                             | 18 (9)                              | 2 (6)                          | >0.99   |
| Vancomycin                              | 6 (3)                               | 0 (0)                          | >0.99   |
| Perioperative surgical pocket irrigation|                                     |                                |         |
| Bacitracin and polymyxin B              | 93 (45)                             | 14 (42)                        | >0.81   |
| Bacitracin, cefazolin, and gentamicin    | 80 (38)                             | 11 (33)                        | 0.57    |
| Bacitracin, polymyxin B, and gentamicin  | 21 (10)                             | 6 (18)                         | 0.23    |
| Bacitracin and ciprofloxacin            | 14 (7)                              | 2 (6)                          | >0.99   |
| Postoperative oral antimicrobials        |                                     |                                |         |
| Cefadroxil                              | 128 (62)                            | 20 (61)                        | 0.92    |
| Trimethoprim/sulfamethoxazole           | 28 (13)                             | 7 (21)                         | 0.28    |
| Clindamycin                             | 21 (10)                             | 3 (9)                          | >0.99   |
| Trimethoprim/sulfamethoxazole and rifampin| 14 (7)                           | 0 (0)                          | 0.23    |
| Augmentin                               | 8 (4)                               | 1 (3)                          | >0.99   |
| Minocycline                             | 5 (2)                               | 1 (3)                          | 0.59    |
| Ciprofloxacin                           | 2 (1)                               | 0 (0)                          | >0.99   |
| None                                    | 2 (1)                               | 1 (3)                          | 0.36    |

Table 4. Concordance Between Prophylactic Antimicrobials and Baseline Axillary Staphylococcus Flora

| Antimicrobial Regimens                  | Noninfected Patients (n = 172)* n (%) | Infected Patients (n = 27)* n (%) | P       |
|-----------------------------------------|-------------------------------------|--------------------------------|---------|
| Perioperative systemic antimicrobials    |                                     |                                |         |
| Discordant                              | 78 (45)                             | 13 (48)                        | 0.79    |
| Concordant                              | 94 (55)                             | 14 (52)                        |         |
| Postoperative oral antimicrobials        |                                     |                                |         |
| Discordant                              | 80 (47)                             | 12 (44)                        | 0.84    |
| Concordant                              | 92 (53)                             | 15 (56)                        |         |

*No bacterial growth (n = 31); No Staphylococcus growth (n = 11).
as diabetes, the use of chemotherapy or radiotherapy, and concurrent axillary lymphadenectomy.6,14,18,19

Sterile surgical and postsurgical aseptic techniques, as well as the use of perioperative chlorhexidine and appropriate timing of perioperative antimicrobials, have all been validated as important pillars for the prevention of SSIs.7,20,21 Unless the patients in our study had a specific β-lactam allergy or due to physicians preference, all received cefazolin which would not provide adequate prophylaxis for those patients colonized with methicillin-resistant Staphylococcus species. Several clinical studies and economic models have compared the use of β-lactam and glycopeptide prophylactic antimicrobials. Although the effectiveness of both of these antimicrobial groups has been shown to be adequate, taking into account environmental selective pressure and the potential for glycopeptide-resistant organisms, these antimicrobials (including vancomycin) are the preferred prophylactic antimicrobials in institutions that have a high prevalence of MRSA infections.22–27 However, there is insufficient evidence to determine whether there is a threshold prevalence of MRSA at which vancomycin would be considered clinically useful and cost-effective.25,26

The use of preoperative MRSA screening and targeted decolonization has also shown promising results in orthopedic and cardiac surgeries.28 However, despite the fact that decolonization is utilized in clinical practice, to our knowledge, there has not been any study evaluating MRSA decolonization in patients undergoing implant-based breast reconstruction. Several other studies have evaluated the use of culture-based targeted antimicrobial prophylaxis for patients colonized with resistant pathogens, instead of the provision of a standardized empiric antimicrobial. For example, it has been shown that the presence of fluoroquinolone-resistant Escherichia coli in rectal swab cultures of patients undergoing transrectal prostate biopsy is a risk factor for subsequent septicemia, but targeted antimicrobial can reduce the risk.10,29 A cost-effectiveness analysis revealed that targeted prophylaxis yielded a cost savings of $4,499 for every infection-related complication of post-transrectal ultrasound-guided prostate biopsy that was averted and that the number needed to treat to prevent 1 infectious complication was 38.11 Targeted antimicrobials have also had favorable results in patients undergoing hepatobiliary reconstruction.30 However, some studies have not been associated with a significant statistical difference between baseline microbial flora, use of targeted antimicrobials, and risk for infection.31

The main limitation of our study is that this was an observational and not an interventional study, in which we were not able to evaluate whether the provision of a targeted antimicrobial prophylaxis based on the patient baseline axillary flora might have decreased the likelihood for SSIs. Additionally, we did not perform cultures from the anterior nares to evaluate whether or not the patients were colonized with MRSA. Furthermore, as several prophylactic antimicrobials utilized during subpectoral surgical pocket irrigation are not commonly tested in routine determinations of antimicrobial susceptibilities, these antimicrobials were not evaluated for concordance.

In summary, after an extended patient follow-up period, we found that the use of concordant or discordant antimicrobials did not impact the risk of SSIs. Therefore, to determine whether targeted antimicrobial prophylaxis based on baseline axillary flora protects against SSIs, a large-scale prospective randomized controlled study is warranted.
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