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Breast

Efficacy of Vancomycin-based Continuous Triple Antibiotic Irrigation in Immediate, Implant-based Breast Reconstruction

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Background: Single irrigation of the peri-implant space with a cefazolin-based triple antibiotic solution is a routine antibiotic prophylaxis measure during implant-based breast augmentation and reconstruction. Cefazolin, however, is less efficacious against resistant *Staphylococcus* species, which are the predominant bacterial species isolated from the peri-implant space. Vancomycin is effective against resistant *Staphylococcus* species and may be a more appropriate prophylactic agent. The availability of single-injection long-acting anesthetic agents allows the novel use of the elastomeric infusion pump for continuous irrigation of antibiotic solution into the peri-implant space. The efficacy of continuous irrigation with a vancomycin-based solution is evaluated here.

Methods: Study patients ($N = 163$; group 1) who underwent immediate, direct-to-implant breast reconstruction received continuous infusion of a vancomycin-based triple antibiotic solution. Patients also received a single injection of liposomal bupivacaine in the pectoralis major/minor muscles for pain control. A historic control group ($N = 113$; group II) received ropivacaine local anesthetic via the infusion pump and a single intraoperative irrigation of the peri-implant space with the vancomycin-based triple antibiotic solution. Incidence of postsurgical infection during the 6 weeks after surgery was compared between the groups.

Results: Group I patients had a statistically significant lower incidence of infections (1.9%) than group II patients (6.4%) ($P = 0.007$). There were no vancomycin-related adverse effects.

Conclusions: Continuous breast irrigation with a vancomycin-based triple antibiotic solution is a safe and effective accompaniment for immediate implant reconstruction. Use of intramuscular anesthetic injection for postoperative pain control allows the elastomeric infusion pump to be available for local tissue antibiotic irrigation.

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INTRODUCTION

Postoperative infection remains a significant complication after breast surgery despite prophylaxis with perioperative systemic antibiotics[1] and intraoperative cefazolin-based triple antibiotic irrigation of the peri-implant space.[2,3] Although these measures have mitigated postoperative infection rates,[4,5] recent studies still report infection rates of up to 30% after implant-based reconstruction.[6,7] Current prophylactic measures are clearly inadequate, and there is a need for more effective measures.

The majority of infectious complications after implant-based reconstructions are due to Gram-positive bacteria.[8] The most frequently isolated bacteria from the peri-implant space are methicillin-resistant *Staphylococcus epidermidis*, methicillin-sensitive *Staphylococcus aureus*, *Pseudomonas* species, and methicillin-resistant *S. aureus*.[8,9] Cefazolin-based antibiotic regimens are not adequate against resistant Staphylococcus.[9] Vancomycin is recognized as being

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the drug of choice for resistant *Staphylococcus* bacteria[10] and may therefore provide more efficacious antibiotic prophylaxis in implant-based surgery.

We have utilized continuous vancomycin-based antibiotic irrigation, delivered via the elastomeric infusion pump, into the peri-implant space as a novel method of infection prophylaxis since 2013. Historically, the elastomeric infusion pump has been primarily used for delivery of local anesthetics into the peri-implant space for pain control. With the advent of single-injection long-acting local anesthetic agents, the infusion pump is no longer needed for pain control and may be repurposed for continuous infusion of antibiotic solution into the peri-implant space.

The purpose of this study is to report on our experience with using vancomycin-based continuous triple antibiotic irrigation of the peri-implant space and its impact on the incidence of postoperative infection compared with vancomycin-based single intraoperative irrigation of the peri-implant space.

PATIENTS AND METHODS

Patient Population

This retrospective analysis included all consecutive patients who underwent immediate, direct-to-implant breast reconstruction from August 2013 to February 2017 in the author's (LMH) practice and received continuous infusion of a vancomycin-based triple antibiotic solution, via an elastomeric pump, into the peri-implant space. Patients who had implant-based flap procedures or expandable implants and those with contraindications to the antibiotic cocktail were excluded from the analysis.

Surgical Technique

A single surgeon performed all reconstructions using a standardized operative procedure under strict sterile conditions. Preoperatively, all patients received 500 mg levofloxacin orally and a single dose of intravenous vancomycin (1 g); the latter was repeated the night of reconstructive surgery and the morning after. Postoperatively, all patients received oral antibiotics—doxycycline 100 mg twice daily for 5 days and levofloxacin 500 mg once daily for 4 days. At the beginning of the reconstructive procedure, patients received a single injection of liposomal bupivacaine (Exparel, Pacira Pharmaceuticals, Inc., Parsippany, N.J.) in the pectoralis major and minor muscles and lateral border of the serratus anterior muscle for pain control. Before the introduction of the implant, the peri-implant space was irrigated once with 400 mL of a triple antibiotic solution consisting of vancomycin 1 g, gentamicin 80 g, and bacitracin 50,000 units in 1 L normal saline. Before subpectoral implant placement was completed, the catheter of the elastomeric pump was inserted through the skin below the inframammary fold and placed along the superior aspect of the subpectoral pocket. When the procedure was completed, the catheter was then connected to the elastomeric infusion system pump (On-Q* pump; Halyard, Irvine, Calif.). Four hundred mL of the same triple antibiotic solution was placed in the pump and delivered at a rate of 4 mL/hr. Two drains were placed in each pocket: one inferiorly under the pectoralis muscle along the lateral and inframammary folds and the other superficially over the muscle/acellular dermal matrix component and underneath the skin flap. Antibiotic irrigation into the peri-implant space was continued for 96 hours postoperatively. Patients were admitted overnight for observation. At discharge, they were taught to remove the catheters and pump on postoperative day 4. Drains were removed when the output was less than 20 mL over a 24-hour period.

Data Collection and Analysis

Study patients (group I) who received continuous vancomycin-based antibiotic irrigation were subcategorized into 2 groups based on implant texture: (1) those who received smooth, round, silicone implants (group I*s*) and (2) those who received textured, anatomic, silicone implants (group I*t*). A cohort of patients who did not receive continuous vancomycin-based antibiotic irrigation were identified from the authors' practice and served as the control population (group II). These patients were consecutive patients who underwent direct-to-implant reconstruction between January 2011 and August 2013. This control group received ropivacaine local anesthetic via the infusion pump for 96 hours. They also received perioperative intravenous vancomycin and oral levofloxacin and postoperative oral antibiotics as in patients in group I. Before the introduction of the implant, the peri-implant space was irrigated once with 400 mL of the same triple antibiotic solution as in group I.

The incidence of postsurgical infection during the 6 weeks after completion of reconstructive surgery was obtained from patient records and compared between groups I and II. Postsurgical infection was identified by the presence of the following signs and symptoms: localized pain/tenderness, fever, erythema, cellulitis, purulent discharge, abscess, and skin dehiscence.[11] Data on patient demographics (age and body mass index), comorbidities (smoking, obesity, diabetes, hypertension), mastectomy characteristics (oncologic, prophylactic, and nipple-sparing), implant characteristics (texture and volume), and adjuvant therapy (preoperative chemo- and/or radiotherapy) use were also obtained, and their contribution to postsurgical infection, if any, was assessed. The time frame for infection assessment was restricted to 6 weeks, as most postsurgical infections occur within this time frame.[12] Infections are also less likely to occur after wound healing, which usually takes 6 weeks. Moreover, late-stage infections are less likely to be implant-related. In addition, after 6 weeks, patients may receive chemotherapy and/or radiation therapy, which may increase the risk of infection and confound the results of this study.

For patient and implant characteristics, comparison between groups I and II was performed using Fisher's exact test for categorical variables and the *t* test for continuous variables. For infectious and other complications, comparison between groups I and II was performed using the nonparametric Pearson chi-square test. This study was approved by the local Institutional Review Board.

RESULTS

Continuous vancomycin-based antibiotic irrigation of the peri-implant space was performed in 316 reconstructions from 163 patients during the study period and constituted group I (Table 1). Of these patients, 87 (171 reconstructions) received smooth round implants (Mentor Corp., Irvine, Calif.; Allergan, Parsippany, N.J.) (group I*s*) and 76 (145 reconstructions) received textured anatomic implants (Allergan, Parsippany, N.J.; Mentor Corp., Irvine, Calif.; Sientra, Inc., Santa Barbara, Calif.) (group I*t*). One hundred and thirteen patients, representing 219 reconstructions, did not receive continuous antibiotic irrigation and formed the control group (group II). All patients in the control group received smooth round implants. Acellular dermal matrix (AlloDerm; LifeCell Corp., Branchburg, N.J.) was used in all reconstructions except in 2 cases in the control group where no matrix was used.

The patient population in groups I and II was well matched (Table 1). There were no significant differences in patient characteristics between the 2 groups with the exception of a significantly higher incidence of hypertension in group II and a trend toward significance of a higher incidence of preoperative radiotherapy in group I.

During the 6-week postoperative period, infections occurred in 6 breasts (1.9%) (5 patients) in group I and 14 breasts (6.4%) (13 patients) in group II (Table 2). The difference in the infection rate between groups I and II was statistically significant (P = 0.007). Among group I breasts, 3 of 6 infections occurred in group I*s* (1.8%) and 3 in group I*t* (2.1%). Group I*s* had a 3.6-fold lower rate of infection than group II, and the difference in the infection rate between groups I*s* and II was statistically significant (P = 0.026). Group I*t* had a 3-fold lower incidence of infection than group II, but the difference did not reach statistical significance (P = 0.056). Of the 6 group I breasts that had an infection, 3 were explanted, 2 were treated with intravenous antibiotics, and 1 was salvaged by running the vancomycin continuous irrigation pump twice after incision and drainage with implant exchange.

Table 1. Patient and Implant Characteristics

Characteristic	Group 1	Group II	*P* value
No. patients	163	113	—
No. reconstructions	316	219	—
Age, y			
Mean (SD)	50.2 (9.7)	49.0 (10.2)	0.323
Range	26.7–69.7	22.4–75.6	—
Body mass index, kg/m^2			
Mean (SD)	23.3 (3.2)	24.0 (3.9)	0.104
Range	17.8–34.0	18.3–37.3	—
Comorbidity, no. patients (%)			
Diabetes	2 (1.2)	4 (3.5)	0.231
Hypertension	9 (5.5)	15 (13.3)	0.03*
Obesity	7 (4.3)	8 (7.1)	0.419
Smoking (current)	3 (1.8)	7 (6.2)	0.097
Laterality, no. patients (%)			
Bilateral	153 (93.9)	106 (93.8)	1.00
Unilateral	10 (6.1)	7 (6.2)	1.00
Mastectomy, no. breasts (%)			
Oncologic	142 (44.9)	108 (49.3)	0.333
Prophylactic	174 (55.1)	111 (50.7)	0.333
Nipple-sparing	262 (82.9)	168 (76.7)	0.078
Chemotherapy, no. patients (%)			
Preoperative	36 (22.1)	15 (13.3)	0.082
Radiotherapy, no. breasts (%)			
Preoperative	9 (2.8)	1 (0.5)	0.051
Implant surface, no. breasts (%)			
Smooth, round	171 (54.1)	219 (100)	1.055×10^{-41}*
Textured, anatomic	145 (45.9)	0	1.055×10^{-41}*
Implant size, mL			
Mean (SD)	556.8 (160.8)	571.2 (152.4)	0.3
Range	215–800	225–800	—

*Statistically significant at $P < 0.05$.

Table 2. Incidence of Infections

Group I: N = 316, *n* (%)	Group I*s*: N = 171, *n* (%)	Group I*t*: N = 145, *n* (%)	Group II: N = 219, *n* (%)
6 (1.9)	3 (1.8)	3 (2.1)	14 (6.4)
χ^2 = 7.26	χ^2 = 4.96	χ^2 = 3.66	—
P = 0.007*	P = 0.026*	P = 0.056	

P values versus group II (control). Group I = patients who received vancomycin-based continuous irrigation; group I*s* = subgroup of patients in group I who received smooth round implants; group I*t* = subgroup of patients in group I who received textured implants; N = no. reconstructions.
*Statistically significant at $P < 0.05$.

Other complications that occurred during the 6-week postoperative period are summarized in Table 3. The incidence of seroma was significantly higher in group I versus group II (4.7% vs 1.4%, P = 0.033) and in group I*t* versus group II (7.6% vs 1.4%, P = 0.033). The incidence of hematoma and skin necrosis was similar between groups I and II. There were no occurrences of vancomycin-associated tissue injury.

The characteristics of patients who had infectious complications are summarized in Table 4. Among the 5 patients who had an infection in group I, none had preoperative chemotherapy, preoperative radiotherapy, or seroma, and none were current smokers. One of 5 patients was obese, 1 had hematoma, and 3 had skin necrosis. Among the 13 patients who had an infection in group II, 2 were obese, 2 were current smokers, 1 had preoperative chemotherapy, 1 had preoperative radiotherapy, 1 had hematoma, 9 had skin necrosis, and none had seroma.

DISCUSSION

Current antibiotic prophylaxis protocols in breast reconstructive surgery include the administration of pre- and postoperative antibiotics and also single intraoperative irrigation of the peri-implant space with a triple antibiotic cocktail.[1–3] Despite these measures, postoperative infection remains a significant concern after breast reconstruction.[6,7] In this study, we have demonstrated that continuous antibiotic irrigation of the peri-implant space with a vancomycin-based triple antibiotic solution for 96 hours is more efficacious in reducing the incidence of postoperative infection than a single irrigation of the peri-implant space with the same antibiotic solution.

Continuous antibiotic irrigation of the peri-implant space is not a novel concept. Continuous antibiotic irrigation has been utilized in other surgical settings, although primarily for the treatment of postsurgical infection. For example, continuous antibiotic irrigation has been uti-

Table 3. Incidence of Other Complications

Complication	Group I: $N = 316$, n (%)	Group Is: $N = 171$, n (%)	Group It: $N = 145$, n (%)	Group II: $N = 219$, n (%)
Hematoma	5 (1.6)	4 (2.3)	1 (0.7)	4 (1.8)
	$P = 0.829$	$P = 0.723$	$P = 0.362$	
	$\chi^2 = 0.0466$	$\chi^2 = 0.126$	$\chi^2 = 0.832$	
Seroma	15 (4.7)	4 (2.3)	11 (7.6)	3 (1.4)
	$P = 0.033$*	$P = 0.474$	$P = 0.003$*	
	$\chi^2 = 4.54$	$\chi^2 = 0.512$	$\chi^2 = 9.12$	
Skin necrosis	19 (6.0)	13 (7.6)	6 (4.1)	18 (8.2)
	$P = 0.323$	$P = 0.823$	$P = 0.125$	
	$\chi^2 = 0.978$	$\chi^2 = 0.0499$	$\chi^2 = 2.36$	

P values versus group II (control). Group I = patients who received vancomycin-based continuous irrigation; group I*s* = subgroup of patients in group I who received smooth round implants; group I*t* = subgroup of patients in group I who received textured implants; *N* = no. reconstructions.
*Statistically significant at $P < 0.05$.

Table 4. Characteristics of Patients with Infection

Characteristic	Group I: $n = 5$	Group II: $n = 13$
Obesity		
Yes	1 (20)	2 (15.4)
No	4 (80)	11 (84.6)
Smoking		
Yes	0 (0)	2 (15.4)
No	5 (100)	11 (84.6)
Preoperative chemotherapy		
Yes	0 (0)	1 (7.7)
No	5 (100)	12 (92.3)
Preoperative radiotherapy		
Yes	0 (0)	1 (7.7)
No	5 (100)	12 (92.3)
Hematoma		
Yes	1 (20)	1 (7.7)
No	4 (80)	12 (92.3)
Seroma		
Yes	0 (0)	0 (0)
No	5 (100)	13 (100)
Mastectomy skin necrosis		
Yes	3 (60)	9 (69.2)
No	2 (40)	4 (30.8)

lized in the salvage of infected nasal cartilage,[13] treatment of aortic graft infection,[14] and treatment of mediastinitis.[15] More recently, Tutela et al. utilized continuous antibiotic irrigation of the peri-implant space after breast reconstruction and reported significant reductions in surgical-site infections and premature explantation.[16] There are, however, important differences between our procedure and that utilized by Tutela et al. that merit mention. First, we utilized a vancomycin-based triple antibiotic solution (vancomycin/gentamicin/bacitracin), whereas Tutela et al. utilized a cefazolin-based solution (cefazolin/gentamicin/bacitracin). Second, we delivered the antibiotic via the pain pump, whereas Tutela et al. utilized a sterile pressure tubing from an arterial line extension kit. Third, continuous irrigation was carried out over 96 hours in our study and over 24 hours in Tutela's study.

Cefazolin-based antibiotics are the current standard prophylaxis regimen used in breast reconstructive surgery.[2,3] Cefazolin, however, is not effective against resistant *Staphylococcus* species, which are the most common bacterial species isolated from the peri-implant space.[8,9] This raises the question as to the appropriateness of utilizing cefazolin for antibiotic prophylaxis in breast reconstruction. Vancomycin, on the other hand, is an effective agent against resistant *Staphylococcus* species.[10] Given that resistant *Staphylococcus* species are a growing concern in hospitals, we believe that a vancomycin-based antibiotic solution is more appropriate for peri-implant space irrigation than a cefazolin-based solution.

The elastomeric pump has been utilized for pain control in breast reconstructive surgery for decades. The pump, however, is becoming obsolete with the availability of intramuscular local analgesic injection. We have found a novel use for this pump in the delivery of continuous antibiotic irrigation. By repurposing the use of this pump, we have also minimized introducing new variables into the reconstructive procedure. The pump usually takes 96 hours to empty, and we kept the same rate of delivery when using it for antibiotic irrigation in this study. The optimal duration of perioperative antibiotic prophylaxis after breast reconstruction remains to be established,[6] but an extended duration is believed to be essential given the compromising characteristics of breast reconstructive surgery, notably, wide undermining, compromised perfusion, placement of implants, and prolonged drain use.[17]

Although an investigation of mechanisms underlying the efficacy of continuous irrigation is beyond the scope of this study, we postulate that a combination of factors may have played a contributory role, including the longer duration of antibiotic prophylaxis, the elimination of surgical debris from the peri-implant space, and the prevention of biofilm formation around implants. Similar to other implantable devices, breast implants foster bacterial colonization. By adhering to the surface of implants and then to each other, bacteria form biofilms around implants.[18] It is conceivable that continuous irrigation may disrupt biofilm formation by interfering with bacterial adhesion to the implant surface. Continuous irrigation also flushes out blood and tissue debris from the peri-implant space, which when retained may provide the nidus for bacterial colonization.

We acknowledge that there are some anecdotal concerns regarding using vancomycin in breasts. First, there have been case reports of tissue necrosis resulting from extravasation of intravenously administered vancomycin,[19,20] which raises the concern for tissue toxicity with vancomycin exposure. It should be noted that intravenous vancomycin is administered at a concentration of 1 g/250 mL of normal saline, whereas the vancomycin-based solution in this study was used at a 4-fold lower concentration (1 g in 1 L of normal saline). At this lower concentration and the concurrent local evacuation by the drains in place, tissue

necrosis or other adverse effects related to vancomycin use were not observed in the over 300 reconstructions performed in this study. Second, vancomycin has a short half-life, which raises questions regarding the stability of the vancomycin-containing antibiotic solution. To address this concern, we performed an in vitro analysis of the stability and compatibility of the 3 antibiotics. At the concentrations used, all 3 appeared to be compatible. Vancomycin and gentamicin have been previously shown to be compatible.[21] The solubility of bacitracin in the presence of the other 2 antibiotics is unknown. However, the purity analysis suggested no one antibiotic influenced the solubility of the others. In addition, particulate formation or color changes were not observed even when the solution was agitated at 3700 rpm, suggesting that the formulation is stable. The pH of the solution also remained relatively consistent with the addition of each antibiotic. Third, although vancomycin is efficacious against resistant *Staphylococcus* species, it has decreased activity against these species if they are embedded in a biofilm.[22] Bacteria embedded in biofilms are resistant to antibiotics that they would otherwise be susceptible to if in suspension.[23] Because vancomycin-based irrigation was used at the time of breast reconstruction in our study, biofilm formation could not yet have occurred at this early time point. Hence, the efficacy of vancomycin against biofilm-embedded, resistant *Staphylococcus* species should not be a concern. On the contrary, the early use of vancomycin may impede biofilm formation as discussed above.

A number of factors are associated with or believed to be associated with an increased risk of postoperative infection, including obesity,[24,25] smoking,[24] preoperative radiotherapy,[26] and preoperative chemotherapy.[9] In our study, the majority of patients who developed infection did not have these risk factors (Table 4). Postoperative complications such as hematoma, seroma, and skin necrosis are also associated with an increased risk of postoperative infection.[9] Again, most patients who had infection in our study did not have hematoma or seroma although they had a higher incidence of skin necrosis (Table 4).

There is some evidence that textured implants may develop a higher load of biofilm[27] and hence may be associated with a higher risk of infections. In our study, among patients in group I, there was no significant difference in the incidence of infection between those who had smooth (group I*s*) and those who had textured (group I*t*) implants (1.8% vs 2.1%, Table 2). Both groups had a lower rate of infection compared with the control group (group II, 6.4%), which had exclusively smooth implants. These data suggest that continuous vancomycin irrigation is efficacious in reducing the risk of infection irrespective of implant surface. This is an interesting finding in light of data that suggest breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is predominantly associated with textured implants[28–30] and that BIA-ALCL appears to have an infectious etiology.[31] A high bacterial load of *Ralstonia* spp. present as a biofilm has been detected in BIA-ALCL specimens.[31] If continuous vancomycin irrigation mitigates biofilm formation, as we postulate, then it is conceivable that it may prevent the pathogenesis of BIA-ALCL. Studies evaluating the impact of continuous vancomycin irrigation and incidence of BIA-ALCL are warranted.

In summary, we have demonstrated that continuous antibiotic irrigation of the peri-implant space with a vancomycin-based solution is both efficacious and safe. The low incidence of postoperative infectious complications may translate to cost savings as infection treatment may require hospitalization for intravenous antibiotics.

CONCLUSIONS

Use of intramuscular injection of liposomal bupivacaine for postoperative pain control allows the elastomeric infusion pump to be available for local tissue antibiotic irrigation. Vancomycin-based triple antibiotic breast irrigation, delivered via the pump, is associated with a low incidence of postoperative infection. Its clinical efficacy and its lack of local tissue injury make this a safe and effective accompaniment for immediate implant reconstruction and are recommended for all implant-based reconstructive procedures.

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REFERENCES

1. Bratzler DW, Dellinger EP, Olsen KM, et al.; American Society of Health-System Pharmacists; Infectious Disease Society of America; Surgical Infection Society; Society for Healthcare Epidemiology of America. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health Syst Pharm.* 2013;70:195–283.
2. Ooi ASh, Song DH. Reducing infection risk in implant-based breast-reconstruction surgery: challenges and solutions. *Breast Cancer (Dove Med Press)* 2016;8:161–172.
3. Adams WP Jr, Rios JL, Smith SJ. Enhancing patient outcomes in aesthetic and reconstructive breast surgery using triple antibiotic breast irrigation: six-year prospective clinical study. *Plast Reconstr Surg.* 2006;118(7 Suppl):46S–52S.
4. Phillips BT, Bishawi M, Dagum AB, et al. A systematic review of antibiotic use and infection in breast reconstruction: what is the evidence? *Plast Reconstr Surg.* 2013;131:1–13.
5. Craft RO, Damjanovic B, Colwell AS. Evidence-based protocol for infection control in immediate implant-based breast reconstruction. *Ann Plast Surg.* 2012;69:446–450.
6. Phillips BT, Halvorson EG. Antibiotic prophylaxis following implant-based breast reconstruction: what is the evidence? *Plast Reconstr Surg.* 2016;138:751–757.
7. Lankiewicz JD, Yokoe DS, Olsen MA, et al. Beyond 30 days: does limiting the duration of surgical site infection follow-up limit detection? *Infect Control Hosp Epidemiol.* 2012;33:202–204.
8. Viola GM, Baumann DP, Mohan K, et al. Improving antimicrobial regimens for the treatment of breast tissue expander-related infections. *Plast Reconstr Surg Glob Open* 2016;4:e704.

9. Feldman EM, Kontoyiannis DP, Sharabi SE, et al. Breast implant infections: is cefazolin enough? *Plast Reconstr Surg.* 2010;126:779–785.
10. Tverdek FP, Crank CW, Segreti J. Antibiotic therapy of methicillin-resistant Staphylococcus aureus in critical care. *Crit Care Clin.* 2008;24:249–60, vii.
11. United States Centers for Disease Control and Prevention. CDC/NHSN surveillance definitions for specific types of infections. January 2017. Available at: http://www.cdc.gov/nhsn/pdfs/pscmanual/17pscnosinfdef_current.pdf. Accessed December 8, 2016.
12. Rubino C, Brongo S, Pagliara D, et al. Infections in breast implants: a review with a focus on developing countries. *J Infect Dev Ctries.* 2014;8:1089–1095.
13. Walton RL, Wu LC, Beahm EK. Salvage of infected cartilage grafts for nasal reconstruction with a through-and-through irrigation system. *Ann Plast Surg.* 2005;54:445–449.
14. Lawrence PF. Conservative treatment of aortic graft infection. *Semin Vasc Surg.* 2011;24:199–204.
15. Shumacker HB Jr, Mandelbaum I. Continuous antibiotic irrigation in the treatment of infection. *Arch Surg.* 1963;86:384–387.
16. Tutela JP, Duncan DP, Kelishadi SS, et al. Continuous postoperative antibiotic irrigation via catheter system following immediate breast reconstruction. *Eplasty* 2015;15:e49.
17. Phillips BT, Wang ED, Mirrer J, et al. Current practice among plastic surgeons of antibiotic prophylaxis and closed-suction drains in breast reconstruction: experience, evidence, and implications for postoperative care. *Ann Plast Surg.* 2011;66:460–465.
18. Costerton JW, Montanaro L, Arciola CR. Biofilm in implant infections: its production and regulation. *Int J Artif Organs* 2005;28:1062–1068.
19. Peyko V, Sasson E. Vancomycin extravasation: evaluation, treatment, and avoidance of this adverse drug event. *Case Rep Intern Med.* 2016;3:40–43.
20. Hoelen DW, Tjan DH, van Vugt R, et al. Severe local vancomycin induced skin necrosis. *Br J Clin Pharmacol.* 2007;64:553–554.
21. Lexi-Comp, Inc. (Lexi-Drugs). Lexi-Comp, Inc. January 29, 2016.
22. Evans RC, Holmes CJ. Effect of vancomycin hydrochloride on Staphylococcus epidermidis biofilm associated with silicone elastomer. *Antimicrob Agents Chemother.* 1987;31:889–894.
23. Donlan RM. Role of biofilms in antimicrobial resistance. *ASAIO J.* 2000;46:S47–S52.
24. McCarthy CM, Mehrara BJ, Riedel E, et al. Predicting complications following expander/implant breast reconstruction: an outcomes analysis based on preoperative clinical risk. *Plast Reconstr Surg.* 2008;121:1886–1892.
25. Gfrerer L, Mattos D, Mastroianni M, et al. Assessment of patient factors, surgeons, and surgeon teams in immediate implant-based breast reconstruction outcomes. *Plast Reconstr Surg.* 2015;135:245e–252e.
26. Francis SH, Ruberg RL, Stevenson KB, et al. Independent risk factors for infection in tissue expander breast reconstruction. *Plast Reconstr Surg.* 2009;124:1790–1796.
27. Jacombs A, Tahir S, Hu H, et al. *In vitro* and *in vivo* investigation of the influence of implant surface on the formation of bacterial biofilm in mammary implants. *Plast Reconstr Surg.* 2014;133:471e–480e.
28. 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.
29. Srinivasa DR, Miranda RN, Kaura A, et al. Global adverse event reports of breast implant-associated ALCL: an international review of 40 government authority databases. *Plast Reconstr Surg.* 2017;139:1029–1039.
30. Loch-Wilkinson A, Beath K, Knight RJW, et al. Breast implant associated anaplastic large cell lymphoma in Australia and New Zealand: high surface area textured implants are associated with increased risk. *Plast Reconstr Surg.* 2017;140:645–654.
31. Hu H, Johani K, Almatroudi A, et al. Bacterial Biofilm infection detected in breast implant-associated anaplastic large-cell lymphoma. *Plast Reconstr Surg.* 2016;137:1659–1669.