



# Salvaging the Infected Breast Tissue Expander: A Standardized Multidisciplinary Approach

George M. Viola, MD, MPH\*

Jesse C. Selber, MD†

Melissa Crosby, MD†

Issam I. Raad, MD\*

Charles E. Butler, MD†

Mark T. Villa, MD†

Steven J. Kronowitz, MD†

Mark W. Clemens, MD†

Patrick Garvey, MD†

Wei Yang, MD‡

Donald P. Baumann, MD†

**Background:** Infections of breast tissue expander (TE) are complex, often requiring TE removal and hospitalization, which can delay further adjuvant therapy and add to the overall costs of breast reconstruction. Therefore, to reduce the rate of TE removal, hospitalization, and costs, we created a standardized same-day multidisciplinary outpatient quality improvement protocol for diagnosing and treating patients with early signs of TE infection.

**Methods:** We prospectively evaluated 26 consecutive patients who developed a surgical site infection between February 2013 and April 2014. On the same day, patients were seen in the Plastic Surgery and Infectious Diseases clinics, underwent breast ultrasonography with or without periprosthetic fluid aspiration, and were prescribed a standardized empiric oral or intravenous antimicrobial regimen active against biofilm-embedded microorganisms. All patients were managed as per our established treatment algorithm and were followed up for a minimum of 1 year.

**Results:** TEs were salvaged in 19 of 26 patients (73%). Compared with TE-salvaged patients, TE-explanted patients had a shorter median time to infection (20 vs 40 days;  $P = 0.09$ ), a significantly higher median temperature at initial presentation [99.8°F; interquartile range (IQR) = 2.1 vs 98.3°F; IQR = 0.4°F;  $P = 0.01$ ], and a significantly longer median antimicrobial treatment duration (28 days; IQR = 27 vs 21 days; IQR = 14 days;  $P = 0.05$ ). The TE salvage rates of patients whose specimen cultures yielded no microbial growth, *Staphylococcus species*, and *Pseudomonas* were 92%, 75%, and 0%, respectively. Patients who had developed a deep-seated pocket infection were significantly more likely than those with superficial cellulitis to undergo TE explantation ( $P = 0.021$ ).

**Conclusions:** Our same-day multidisciplinary diagnostic and treatment algorithm not only yielded a TE salvage rate higher than those previously reported but also decreased the rate of hospitalization, decreased overall costs, and identified several clinical scenarios in which TE explantation was likely. (*Plast Reconstr Surg Glob Open* 2016;4:e732; doi: 10.1097/GOX.0000000000000676; Published online 10 June 2016.)

owing to favorable economic factors, improvements in implant design, and the widespread successful use of acellular dermal matrix, breast reconstruction with tissue expanders (TEs) and im-

plants is becoming increasingly popular among breast cancer patients who have undergone mastectomy.<sup>1,2</sup> The rate of breast reconstruction has increased steadily during the past several years; the American Society

From the Departments of \*Infectious Diseases, †Plastic Surgery, and ‡Radiology, The University of Texas MD Anderson Cancer Center, Houston, Tex.

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of Plastic Surgeons reported that more than 90,000 patients in the United States underwent breast reconstruction in 2013 alone.<sup>3</sup> Of these patients, approximately 70,000 underwent breast reconstruction with a TE, whereas the remaining patients had autologous reconstructions. The advantages of TE-based breast reconstructions include the potential for enhanced aesthetic outcomes and rapid postoperative recovery with minimal morbidity and functional limitation.<sup>4</sup>

Unfortunately, the rate of infection after breast TE reconstruction remains unacceptably high, ranging from 2.5% to 24%.<sup>5-9</sup> During the past 10 years, our infection rate was approximately 12%. These infections are complex and severe, and patients whose TE infections do not respond to antibiotic treatment alone usually require further surgery and explantation of the device. We have estimated that at our institution, patients who developed an implant-based reconstructive breast infection required explanation of the TE in 50% of the occasions. The eventual loss of the TE is a significant complication that can delay further adjuvant radiation and chemotherapy and require a more complicated reconstruction in the future.<sup>10,11</sup> The estimated medical and surgical costs of treating a patient who has an infected TE can surpass tens of thousands of dollars.<sup>12</sup> In addition, rather than being cared for in an outpatient setting, to expedite care, patients with skin soft tissue inflammatory (SSTI) processes are commonly hospitalized, which further increases the costs. Therefore, to reduce the rate of TE removal, hospitalization, and overall costs at our institution, we created a standardized same-day multidisciplinary protocol for diagnosing and treating patients with early signs of TE infection. Herein, we describe the implementation of this protocol and our initial investigation of patient factors potentially associated with TE explantation.

## METHODS

### Patients and Protocol

As part of our institution's Clinical Safety and Effectiveness program, and after several meetings among Plastic Surgery, Radiology, and Infectious Diseases specialists, we created a same-day multidisciplinary clinic for managing breast TE-related infections in the outpatient setting. We prospectively evaluated all patients who had undergone mastecto-

my followed by TE reconstruction at our institution. Consecutive patients who were hemodynamically stable, presented with early signs of a postsurgical site infection to the Plastic Surgery Department between February 2013 and April 2014, and did not require immediate hospitalization were included in the study. We utilized the Centers for Disease Control and Prevention definition of a surgical site infection involving an implant.<sup>13</sup> All patients were evaluated and treated according to our standardized diagnostic and treatment algorithm (Fig. 1A and B). Every patient was scheduled to undergo same-day outpatient breast ultrasonography with periprosthetic fluid aspiration, as necessary followed by a consultation with the Infectious Diseases Department outpatient clinic. Aspirated periprosthetic fluid specimens were submitted for routine cytological studies and bacterial, fungal, and acid-fast bacilli stains and cultures. Thereafter, on the basis of ultrasonography findings, initial microbiological staging studies, and our institutional postoperative microbiological database, patients were prescribed a standardized biofilm active antimicrobial regimen that empirically targeted methicillin-resistant *Staphylococcus spp.* and *Pseudomonas spp.*, the organisms that most commonly cause TE infections (Fig. 2). This study was approved by MD Anderson's Quality Improvement Assessment Board.

### Statistical Analysis

Descriptive statistics are presented as medians with first and third quartiles (Q1–Q3) for continuous variables and as frequencies with percentages for categorical variables. Differences in continuous variables between patients whose TEs were salvaged and patients who underwent TE explantation were assessed using the Wilcoxon rank-sum test. Differences in categorical variables between the groups were assessed using the chi-square or Fisher exact test, as appropriate. All tests were 2 sided, and *P* values of 0.05 or less were considered significant. The statistical analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, N.C.).

## RESULTS

### Clinical and Surgical Characteristics

Twenty-six patients were evaluated and included in our diagnostic and treatment protocol (Table 1). At the time of initial surgery, 14 patients (54%) had an invasive breast carcinoma, 11 (42%) had an in situ carcinoma, and 1 (4%) had no cancer but underwent a prophylactic mastectomy owing to breast cancer susceptibility genes positivity. Only 4 patients (15%) had received neoadjuvant hormonal therapy, 2 (8%) had received neoadjuvant chemotherapy,

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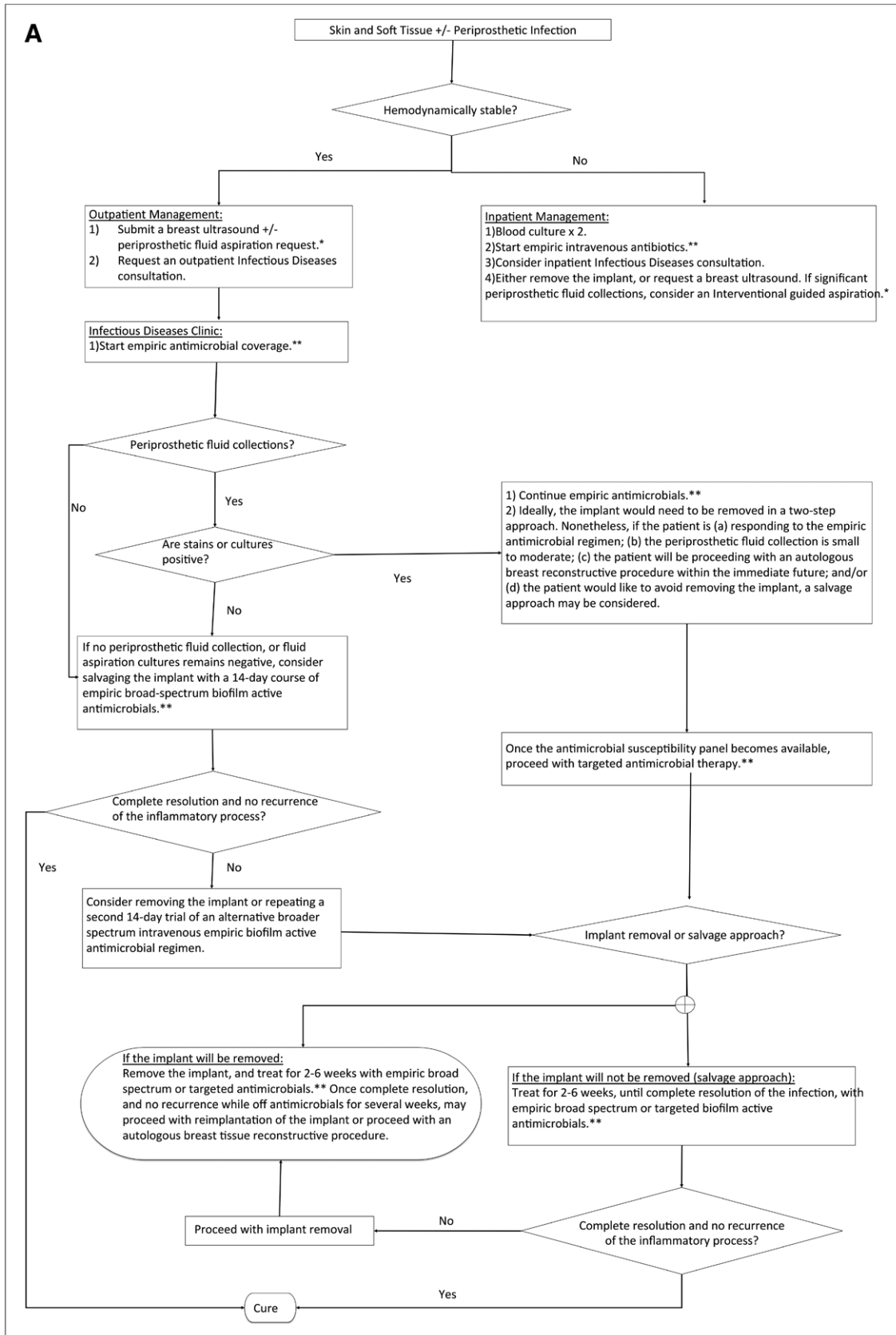


Fig. 1. (Continued).

**B \* Breast Ultrasound +/- Periprosthetic Fluid Aspiration Request:**

1) Submit an outpatient breast ultrasound request, and specify the reason: "Rule out periprosthetic breast fluid collection. If fluid collection to be found, please aspirate fluid, and submit for cytological analysis, as well as bacterial, fungal, acid-fast bacillus stains and cultures."

**\*\* Antimicrobial Recommendations:**

1) Antimicrobial allergies: Prior to the provision of antimicrobials, asses for any antimicrobial allergies.

2) Route of antimicrobial recommendation: Although the extend and severity of the infection should weight on the route of antimicrobial administration, the choice of either oral or intravenous antimicrobials should be left up to the treating physician.

3) Empiric antimicrobial coverage: Before the availability of the culture results, based on our historical institutional culture data, provision of adequate antimicrobial coverage, should be provided for: Methicillin-resistant staphylococcus and Gram-negative rods, including Pseudomonas.

4) Targeted antimicrobial coverage: Once the culture and antimicrobial susceptibility panel results are made available, readjust or deescalate the antimicrobial coverage to cover the offending microorganism.

5) Provision of appropriate biofilm active antimicrobials: If the tissue expander (TE) is being removed, it is not necessary to provide biofilm active antimicrobials. Nonetheless, if the device is left in place, or the intention is to salvage the TE, please provide antimicrobials with adequate biofilm penetration (see below). Lastly, the addition of rifampin should be considered to the empiric antimicrobial, or the targeted antimicrobial regimen choice, specifically if the latter reveals a rifampin sensitive staphylococci.

Empiric and Targeted Antimicrobial Recommendations				
	Empiric Antimicrobials		Targeted Antimicrobials (should provide coverage towards the offending organism)	
	Device to be removed	Device not to be removed (salvage regimen)	Device to be removed	Device not to be removed (salvage regimen)
Oral Regimen	Minocycline/ Linezolid + Ciprofloxacin.	Minocycline + Ciprofloxacin + Rifampin.	If a <b>Gram-negative rod</b> is recovered, if possible, please choose a beta-lactam or a quinolone.	If a <b>Gram-negative rod</b> is recovered, if possible, a quinolone should be selected over a beta-lactam.
Intravenous Regimen	Vancomycin/ Daptomycin + Meropenem/ Cefepime.	Minocycline/ Daptomycin + Meropenem/ Cefepime + Rifampin.	If <b>Methicillin-Resistant Staphylococcus</b> is recovered, if possible select Minocycline/ Linezolid/ Vancomycin/ Daptomycin.  If <b>Methicillin-Sensitive Staphylococcus</b> is recovered, if possible ideally select Dicloxacillin or Nafcillin over Minocycline/ Linezolid/ Vancomycin or Daptomycin.  If <b>Candida</b> is recovered, an echinocandin or azole should be selected over a Polyene.	If <b>Staphylococcus</b> is recovered, Minocycline or Daptomycin + Rifampin, should be chosen over Linezolid or Vancomycin.  If <b>Candida</b> is recovered, an echinocandin or azole should be selected over a Polyene.

**Fig. 1.** A and B, Breast tissue expander–related infection diagnostic and treatment algorithm.

and 1 (4%) had received neoadjuvant radiotherapy. A total of 11 patients had a unilateral TE placement (42%), whereas 15 patients (58%) had a bilateral TE placement. Skin-sparing mastectomy was performed in all patients, of whom 21 (81%) had an immediate 1-step reconstruction and 5 (19%) had a delayed 2-step reconstruction. Most patients (77%) underwent a sentinel lymph node biopsy, and 6 (23%) underwent complete axillary lymph node dissection. A bioprosthetic mesh was utilized for lower pole support in 11 patients (42%). Postsurgically, 9 patients (35%) had received adjuvant chemotherapy, and 4 patients (15%) had received adjuvant radiation therapy.

Of the 26 patients in this study, 19 (73%) had their TE salvaged, whereas 7 (27%) had their TE explanted. The overall demographics and clinical and surgical characteristics of the patients who had their TE salvaged and those who underwent TE

explantation did not differ significantly ( $P > 0.22$ ). However, patients who had their TE explanted had a higher incidence of bioprosthetic mesh use (71% vs 32%), but this difference did not reach significance ( $P = 0.09$ ).

**Infection Characteristics**

The median time from TE placement to infection for all patients was 38 days (Q1–Q3 = 20–53 days). The median time to infection of the TE-salvaged group (40 days) was longer than that of the TE-explanted group (20 days), but this difference was not significant ( $P = 0.09$ ). The median time from the manifestation of clinical symptoms of infection to the initial Plastic Surgery visit was 3 days (Q1–Q3, 2–7 days), and subsequent visit from the Plastic Surgery to the Infectious Diseases outpatient clinic was obtained within the same day. The median time from symptoms of infection to the outpatient clinic visit

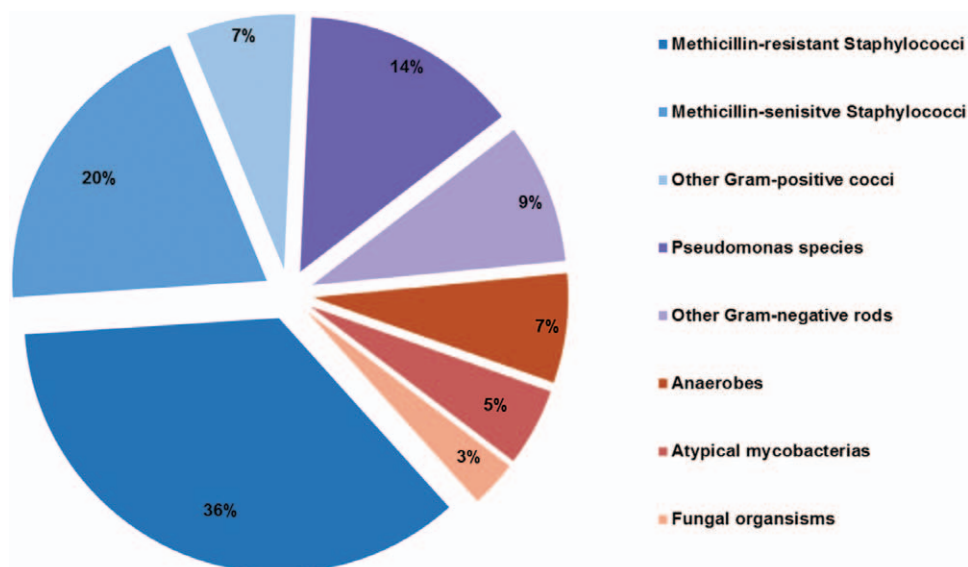


Fig. 2. Microbiology of breast tissue expander-related infections.<sup>14</sup>

between the TE-salvaged and TE-explanted groups did not differ significantly ( $P = 0.48$ ). All patients had received postoperative oral prophylactic antimicrobials, whereas only 5 patients (19%) were receiving prophylactic postoperative antibiotics at the time

of infection. The median temperature at the time of the initial clinical visit of the TE-salvaged group (98.3°F; Q1–Q3 = 98.0–98.4°F) was significantly lower than that of the TE-explanted group (99.8°F; Q1–Q3 = 98.4–100.5°F;  $P = 0.01$ ). The median white

Table 1. Clinical and Surgical Characteristics

Variable	Total (n = 26)	TE Salvaged (n = 19)	TE Explanted (n = 7)	P
Median age, years (Q1–Q3)	50 (42–60)	50 (41–61)	53 (42–59)	0.84
Race	—	—	—	0.89
White	14 (54)	10 (53)	4 (57)	—
Black	6 (23)	3 (16)	2 (29)	—
Hispanic	6 (23)	5 (26)	1 (14)	—
Asian	1 (4)	1 (5)	0	—
Diabetes	1 (4)	0 (0)	1 (14)	0.27
Active smoker	0	0	0	N/A
Median BMI, kg/m <sup>2</sup> (Q1–Q3)	30.9 (26.4–36.5)	30.7 (26.4–35.3)	31.2 (21.5–40.5)	0.51
Breast diagnosis	—	—	—	0.22
No cancer; BRCA positive	1 (4)	1 (5)	0	—
In situ carcinoma	11 (42)	6 (32)	5 (71)	—
Invasive carcinoma	14 (54)	12 (63)	2 (29)	—
Neoadjuvant treatment	—	—	—	—
Hormonal therapy	4 (15)	2 (11)	2 (29)	0.29
Chemotherapy	2 (8)	1 (5)	1 (14)	0.47
Radiotherapy	1 (4)	1 (5)	0	>0.99
Skin-sparing mastectomy	26 (100)	19 (100)	7 (100)	N/A
Time of reconstruction	—	—	—	>0.99
Immediate	21 (81)	15 (79)	6 (86)	—
Delayed	5 (19)	4 (21)	1 (14)	—
Tissue expander brand	—	—	—	0.67
Mentor	14 (54)	11 (79)	3 (21)	—
Allergan	12 (46)	8 (67)	4 (33)	—
Bioprosthetic mesh	11 (42)	6 (32)	5 (71)	0.09
Lymph node dissection	—	—	—	>0.99
Sentinel lymph node biopsy	20 (77)	15 (79)	5 (71)	—
Axillary lymph node dissection	6 (23)	4 (21)	2 (29)	—
Adjuvant treatment	—	—	—	—
Chemotherapy	9 (35)	8 (42)	1 (14)	0.36
Radiotherapy	4 (15)	4 (21)	0	0.55

All data are presented as no. patients (%) unless otherwise indicated.

BMI, body mass index; BRCA, breast cancer susceptibility genes; N/A, not applicable.

blood cell count was 6350 cells/ $\mu$ l (Q1–Q3 = 4500–7800 cells/ $\mu$ l), and only 2 patients were neutropenic at the time of infection. The median drainage catheter time was 22 days (Q1–Q3 = 14–32 days), with 12 patients (46%) having a catheter in place at the time of infection. The proportion of TE-explanted patients (86%; 6 of 7 patients) who had a drainage catheter in place at the time of infection was significantly higher than the proportion of TE-salvaged patients (32%; 6 of 19 patients) who had a catheter in place at the time of infection ( $P=0.026$ ; Table 2).

As per our algorithm, all patients underwent breast ultrasonography before their consultation in the outpatient Infectious Disease clinic. Of the 19 TE-salvaged patients, 8 (42%) had no visible periprosthetic fluid on ultrasonography, whereas all 7 TE-explanted patients had ultrasonographic evidence of fluid around the TE, of whom 5 (71%) of these patients had a sufficiently large fluid col-

lection to warrant ultrasonography-guided fluid aspiration ( $P=0.10$ ). Overall, 13 patients underwent ultrasonography-guided fluid aspiration. Although none of the aspiration specimens was purulent in appearance, 10 grew microorganisms, which included *Pseudomonas spp.* (4 cases), *Staphylococcus lugdunensis* (2 cases), *Propionibacterium* (2 cases), methicillin-sensitive *Staphylococcus aureus* (1 case), and *Staphylococcus epidermidis* (1 case). Among the TE-explanted patients, cultures obtained at the time of explantation grew *Pseudomonas spp.* (3 cases), *S. lugdunensis* (1 case), and nothing (3 cases). All intraoperative cultures were concordant with the ultrasonography-guided fluid aspiration specimen cultures.

Compared with patients who had a superficial SSTI, patients who had a deep-seated periprosthetic infection were significantly more likely to undergo TE explantation ( $P=0.021$ ). Furthermore, the TE salvage rate after infection was 92% among patients whose flu-

**Table 2. Infection Characteristics**

Variable	Total (n = 26)	TE Salvaged (n = 19)	TE Explanted (n = 7)*	P
Median time from TE placement to infection, d (Q1–Q3)	38 (20–53)	42 (25–90)	20 (13–40)	0.09
Median time from clinical symptoms to initial plastic surgery visit, d (Q1–Q3)	3 (2–7)	3 (1–7)	4 (2–14)	0.48
Median time from initial plastic surgery visit to infectious diseases visit, d (Q1–Q3)	1 (1–1)	1 (1–1)	1 (1–1)	0.60
Timing of postoperative prophylactic antibiotics	—	—	—	—
Any	26 (100)	19 (100)	7 (100)	N/A
At time of infection	5 (19)	4 (21)	1 (14)	>0.99
Median drainage catheter time, d (Q1–Q3)	22 (14–32)	24 (15–32)	14 (12–40)	0.42
Drainage catheter in place at time of infection	12 (46)	6 (32)	6 (86)	0.026
Median maximum temperature at time of consult, °F (Q1–Q3)	98.4 (98.2–98.8)	98.3 (98.0–98.4)	99.8 (98.4–100.5)	0.011
Median WBC count at time of consult, cells k/ $\mu$ l (Q1–Q3)	6.35 (4.5–7.8)	6.2 (4.2–7.8)	7.2 (5.3–9.4)	0.22
Neutropenia at time of infection	2 (8)	2 (11)	0	>0.99
Ultrasonography performed	26 (100)	19 (100)	7 (100)	N/A
Ultrasonography findings	—	—	—	0.10
No fluid	8 (31)	8 (42)	0	—
Yes and fluid, not aspirated	5 (19)	3 (16)	2 (29)	—
Yes and fluid, aspirated†	13 (50)	8 (42)	5 (71)	—
Aspirated fluid appearance	—	—	—	—
Serous	4 (31)	2 (11)	2 (29)	0.29
Hemorrhagic	2 (15)	2 (11)	0	>0.99
Serous hemorrhagic	7 (54)	4 (21)	3 (43)	0.34
Purulent	0	0	0	N/A
Type of infection	—	—	—	0.021
Superficial	15 (58)	14 (74)	1 (14)	—
Deep seated	11 (42)	5 (26)	6 (86)	—
Microorganisms recovered	13 (50)	7 (37)	6 (86)	0.07
<i>Pseudomonas spp.</i>	4 (31)	0	4 (57)	0.0023
<i>Staphylococcus epidermidis</i>	3 (23)	2 (11)	1 (14)	>0.99
<i>Staphylococcus lugdunensis</i>	3 (23)	2 (11)	1 (14)	>0.99
MSSA	2 (15)	2 (11)	0	>0.99
<i>Propionibacterium spp.</i>	1 (8)	1 (5)	0	>0.99

All data are presented as no. patients (%) unless otherwise indicated.

\*Of the 7 TE-explanted patients on antimicrobials, 4 had positive cultures.

†Of the 13 patients who underwent ultrasonography-guided fluid aspiration, 10 had cultures positive for *Pseudomonas spp.* (4 cases), *S. lugdunensis* (2 cases), *Propionibacterium* (2 cases), MSSA (1 case), or *S. epidermidis* (1 case).

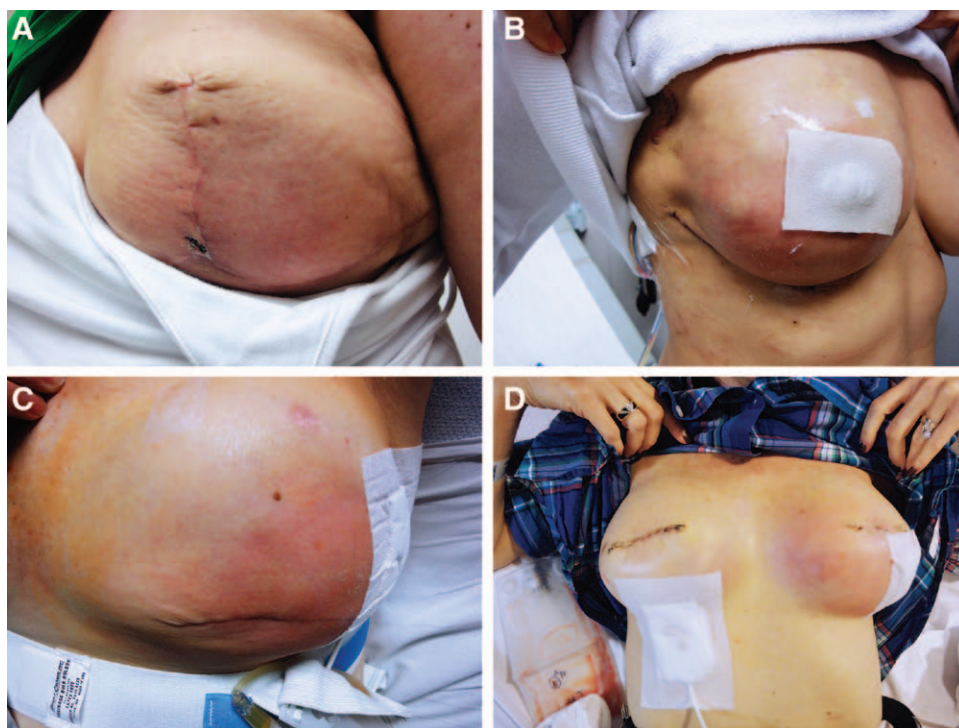
MSSA, methicillin-sensitive *Staphylococcus aureus*; N/A, not applicable; WBC, white blood cell.

id specimen cultures had no microbial growth, 75% among patients with *Staphylococcus spp.* growth, and 0% among patients with *Pseudomonas spp.* growth. None of the TE-salvaged patients required inpatient hospitalization. After the initial infection was adequately treated, 95% of the TE-salvaged patients and 86% of the TE-explanted patients underwent successful definite breast reconstruction ( $P = 0.47$ ). Except for 1 patient within the salvaged group who passed away because of metastatic diseases, all other patients proceed with definitive breast reconstruction, whereas in the explanted group, 4 patients proceeded with a second TE placement followed by a permanent implant reconstruction, 2 patients had a myocutaneous flap reconstruction, and 1 patient desired not to proceed with any further reconstruction. The overall median time to final reconstruction was 104 days (Q1–Q3 = 44–203 days); the difference in time to final reconstruction between the TE-salvaged (Q1–Q3 = 40–192 days) and TE-explanted patients (Q1–Q3 = 78–371 days) did not differ significantly ( $P = 0.44$ ).

#### Empiric and Specific Antimicrobial Regimens

Immediately after their presentation to the Infectious Diseases outpatient clinic, 19 patients (73%) were started on an empiric oral antimicrobial regimen and 7 patients (26%), based on infection

severity (Fig. 3), were started on an intravenous regimen (Table 3). The most commonly utilized empiric oral regimen was minocycline, ciprofloxacin, and rifampin (14 cases), and the most common combined intravenous and oral regimen was daptomycin, ceftipime and rifampin (4 cases), or daptomycin, ciprofloxacin and rifampin (2 cases). After completing an initial course of oral antimicrobials, 9 patients (35%) did not receive additional antimicrobials, 4 patients (15%) continued on an oral regimen, and 6 patients (23%) were transitioned to an intravenous regimen. Among the remaining 7 patients (27%), who were started on an empiric intravenous antimicrobial regimen, 2 patients (8%) did not receive additional antimicrobials, 4 (15%) continued on an oral regimen, and 1 (4%) continued on an intravenous regimen. Patients who were started on either an oral or intravenous regimen and who did not receive additional antibiotics or who continued on an oral regimen had a TE salvage rate of 84%. In contrast, patients who were started on an oral or intravenous regimen who continued on an intravenous regimen, because of the progression or persistence of infection, had a TE salvage rate of only 42%. However, the difference in salvage rate between these 2 groups was not significant ( $P = 0.057$ ). Furthermore, the TE salvage rate of patients in whom an organism was identified



**Fig. 3.** Initial presentation of 4 patients with breast tissue expander–related infections. The patients in (A) and (B) had mild local infections and were started on an oral antibiotic regimen, whereas those in (C) and (D) had moderate to severe local infections and were started on an empiric intravenous antimicrobial regimen.

**Table 3. Antimicrobial Regimens Utilized\***

Variable	Total (n = 26)	TE Salvaged (n = 19)	TE Explanted (n = 7)	P
Initial antimicrobial regimen	—	—	—	>0.99
Oral	19 (73)	14 (74)	5 (71)	—
Intravenous	7 (27)	5 (26)	2 (29)	—
Continuation of antimicrobials, by route of administration				
Oral to none	9 (35)	7 (37)	2 (29)	>0.99
Oral to oral	4 (15)	4 (21)	0 (0)	0.55
Oral to intravenous	6 (23)	3 (16)	3 (43)	0.29
Intravenous to none	2 (8)	2 (11)	0	>0.99
Intravenous to oral	4 (15)	3 (16)	1 (14)	>0.99
Intravenous to intravenous	1 (4)	0	1 (14)	0.27
Continuation of antimicrobials, by specific coverage	—	—	—	0.021
Empiric	15 (58)	14 (74)	1 (14)	—
Empiric to targeted	11 (42)	5 (26)	6 (86)	—
Median total antibiotic time, days (Q1–Q3)	22 (18–28)	21 (14–28)	28 (22–49)	0.05

All data are presented as no. patients (%) unless otherwise indicated.

\*A review of the antimicrobial susceptibility panel of all specimens recovered via ultrasonography-guided aspiration or intraoperatively revealed that all microorganisms were adequately covered with the initial empiric antimicrobial regimen.

and the empiric regimen was transitioned to a specific targeted antimicrobial regimen (45%) was significantly lower than that of patients who received an empiric regimen only (92%;  $P = 0.021$ ). The median antimicrobial treatment duration of the TE-explanted patients (28 days, Q1–Q3 = 22–49 days) was significantly longer than that of the TE-salvaged patients (21 days, Q1–Q3 = 14–28 days;  $P = 0.05$ ).

### DISCUSSION

Our same-day multidisciplinary coordinated algorithm for diagnosing and treating SSI was associated with an overall TE salvage rate of 73%. This rate is substantially higher than our 50% historical success rate and than those reported in other studies, which have ranged from 25% to 64%.<sup>15,16</sup> The higher TE salvage rate has also represented a substantial cost savings. We estimated that the average medical expense for managing a breast TE inflammatory infectious process, including a 5-day hospital stay and follow-up in the outpatient setting for an additional 9 days, ranges from \$18,500 to \$28,000. However, the cost to care for a patient in our outpatient protocol was approximately \$3500 if the patient was treated with oral antimicrobials and approximately \$11,500 if the patient was treated with intravenous antimicrobials.

The implementation of the protocol we describe herein takes into account myriad factors that must be considered when caring for patients with TE infections. The measures to prevent a TE infection include perioperative antimicrobials, intraoperative antibiotic irrigation, and prolonged postoperative oral antimicrobials. Despite these measures, the rate of TE infection among mastectomy patients undergoing TE-based breast reconstruction remains unacceptably high, ranging from 2.5% to 24%.<sup>5–9</sup> This

rate is considerably higher than the <1% to 2.5% reported for patients who have undergone other implant-based procedures such as routine breast augmentation.<sup>10,11,17–19</sup> Multiple risk factors can increase the risk of TE-related infections in patients who undergo breast reconstruction, including perioperative chemotherapy, perioperative radiotherapy,<sup>5,9,20</sup> tobacco use,<sup>21</sup> diabetes mellitus,<sup>22</sup> a body mass index of more than 25 kg/m<sup>2</sup>, a breast cup size greater than C,<sup>5,21</sup> axillary lymph node dissection,<sup>5,9</sup> use of acellular dermal matrix,<sup>4</sup> immediate breast reconstruction,<sup>5,7</sup> bilateral breast reconstruction,<sup>5,7</sup> use of surgical drains,<sup>23,24</sup> mastectomy skin flap necrosis,<sup>22</sup> use of bevacizumab,<sup>25</sup> and adjuvant chemotherapy after immediate reconstruction.<sup>25,26</sup> Therefore, at the first sign of an SSTI, treating the infection and quickly coordinating the treatment approach among reconstructive surgeons, interventional radiologists, and infectious disease specialists is paramount to optimize the potential for TE salvage. If the SSTI is not adequately treated immediately, with an appropriate antimicrobial covering the most common pathogen, the infection can progress and form a mature biofilm on the TE, thereby increasing the probability of TE loss.<sup>27</sup> It is not unusual for a patient to be initiated on a narrow-spectrum antimicrobial regimen that does not cover the most common organisms causative for a reconstructive breast site infection, such as amoxicillin-clavulanate, cephalexin, trimethoprim-sulfamethoxazole, or clindamycin. Furthermore, any periprosthetic fluid specimens obtained via the drainage catheter or ultrasound guided aspiration should be submitted for routine bacterial, fungal, and acid-fast bacilli stains and cultures to identify the specific microorganism.<sup>17,28</sup> Until the organism is identified, the patient should receive an empiric antimicrobial



regimen that covers the organisms that most commonly cause TE infection and that are active against biofilm-embedded organisms.

The decision to initiate either an oral or intravenous regimen in the outpatient setting is a subjective decision, which is determined mainly by the severity of the patient's clinical presentation. At our institution, methicillin-resistant staphylococci and Gram-negative rods, including *Pseudomonas spp.*, are responsible for 60% of TE infections, and our empiric antimicrobial regimen is designed to target these organisms.<sup>14</sup> For empiric methicillin-resistant staphylococci coverage, because tetracycline plus rifampin or daptomycin plus rifampin are able to penetrate the biofilm matrix and remain active against the biofilm-embedded organism, these should be selected over vancomycin or linezolid.<sup>29–32</sup> To avoid rifampin resistance and based on several in vitro and in vivo studies to synergize other antimicrobials, rifampin should not be used alone, but in combination with 1 of the anti-Gram-positive drugs mentioned earlier.<sup>33–36</sup> In addition, because it fulfills the aforementioned antibiotic criteria, for empiric Gram-negative coverage, a quinolone such as ciprofloxacin should be selected over a  $\beta$ -lactam such as piperacillin, cefepime, or imipenem.<sup>37–40</sup> If a microorganism is eventually identified, the empiric antimicrobial regimen should be transitioned to one that is active within the biofilm matrix and specifically targets the identified organism.

Our study yielded several key insights regarding the management of TE infections. First, the use of bioprosthetic mesh, which has been associated with an increased rate of seromas and hematomas, was more common among TE-explanted patients than TE-salvaged patients (71% vs 32%;  $P = 0.09$ ). Accordingly, a significantly higher proportion of TE-explanted patients had a drainage catheter in place at the time of infection (86% vs 32%;  $P = 0.026$ ). Therefore, although biological meshes can be used in breast reconstruction to provide or enhance lower pole breast support, their potential increased risk for seromas, extended drainage use, and risk for infection should also be considered.<sup>4,41</sup> Second, postoperative infections in TE-explanted patients tended to occur earlier than those in TE-salvaged patients (median time to infection, 20 vs 40 days;  $P = 0.09$ ), likely because such infections were because of microorganisms with higher virulence and/or bacterial inoculation. Third, patients who presented with systemic symptoms, including a temperature above 98.4°F, were more likely than patients who did not present with systemic symptoms to undergo TE explantation ( $P = 0.01$ ). Although

we found no significant difference in white blood cell count between TE-explanted and TE-salvaged patients, Reish et al<sup>16</sup> reported that TE-explanted patients have a significantly higher white blood cell count than TE-salvaged patients do ( $P = 0.0001$ ), which suggests that TE salvage should likely be discouraged in patients with a high white blood cell count. Fourth, as has been similarly reported for other device-related infections,<sup>36,42,43</sup> we also found that patients whose periprosthetic fluid specimens were grossly purulent or were positive for *Pseudomonas* were more likely to undergo TE explantation, likely because these organisms create a complex, well-entrenched biofilm matrix that makes TE salvage exceedingly difficult if not impossible. This finding adds to existing evidence that TE salvage should be discouraged in such patients.<sup>16</sup> In contrast to other studies,<sup>15,16</sup> we found that the TE explantation rates of patients with staphylococci infections did not differ significantly, likely because of the prompt initiation of adequate antimicrobials and subsequent prevention of mature biofilm formation. Fifth, regardless of whether the initial empiric regimen consisted of an oral or intravenous formulation, the TE salvage rate of patients who were continued on an extended course of intravenous antimicrobials (42%) was half that of patients who were continued on solely an oral antibiotic regimen or who discontinued antimicrobial treatment after completing their initial regimen (84%;  $P = 0.057$ ). The absence of a prompt and complete resolution of the infection within 14-days, and requiring an extension of the antibiotic course or requiring switching to an intravenous regimen, most likely reflects the severity of the infection and low likelihood of TE salvage.

The potential limitations of this study included its single-center design and small patient sample. Despite these limitations, this prospective study highlights how a prompt, coordinated, multidisciplinary approach can be used to successfully treat patients with TE-related infections in the outpatient setting while improving outcomes and reducing costs. This study also identifies several clinical scenarios in which TE salvage would be unlikely, including those involving an early infection postoperatively, the presence of a drainage catheter, and fever. In addition, our findings indicate that extending the antimicrobial treatment and neglecting to identify patients who have a high likelihood of TE explantation potentially results in an extended treatment course, complete with its increased costs, and potential delay of adjuvant radiotherapy and/or chemotherapy in patients with locally advanced breast cancer. Therefore, following our standardized rapid diagnostic and treat-

ment algorithm at the first sign of infection, thereby preventing the progression of the infection to the deep tissues or TE, should increase the probability of TE salvage and decrease the overall cost of care.

## CONCLUSIONS

In the era of complex medical device–related infections, decreasing medical care reimbursement, and emphases on clinical outcomes and patient safety, one must take an evidence-based, interdisciplinary, patient-centered approach to treating TE-related infections. The implementation of a same-day multidisciplinary clinic that utilizes hospital epidemiology-based empiric therapy, ultrasonography, periprosthetic fluid aspiration, and culture-directed antimicrobial therapy to manage TE-related infections should improve the TE salvage rate, decrease the care costs, and improve the outcomes of patients who have undergone TE-based breast reconstruction. We encourage other physicians and institutions to enhance the salvage rate of infected TE by following our multidisciplinary diagnostic and treatment algorithm.

**George M. Viola, MD, MPH**

Division of Internal Medicine  
Department of Infectious Diseases  
Unit 1460

The University of Texas MD Anderson Cancer Center  
1515 Holcombe Boulevard  
Houston, TX 77030  
E-mail: GMViola@mdanderson.org

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