

# Prophylactic Antibiotics for Deep Inferior Epigastric Perforator Flap Breast Reconstruction: A Comparison between Three Different Duration Approaches

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**Background:** There is no consensus on the duration of prophylactic antibiotic use for autologous breast reconstruction after mastectomy. We attempted to standardize the use of prophylactic antibiotics after mastectomy using a deep inferior epigastric perforator flap for the breast reconstruction procedure.

**Methods:** This retrospective case series included 108 patients who underwent immediate breast reconstruction with a deep inferior epigastric perforator flap at the Ditmanson Medical Foundation Chia-Yi Christian Hospital between 2012 and 2019. Patients were divided into three groups based on the duration of prophylactic antibiotic administration (1, 3, and >7 days) for patients with drains. Data were analyzed between January and April 2021.

**Results:** The prevalence of surgical site infection in the breast was 0.93% (1/108), and in the abdomen it was 0%. The patient groups did not differ by age, body mass index, smoking status, or neoadjuvant chemotherapy. Only one patient experienced surgical site infection in the breast after half-deep necrosis of the inferior epigastric perforator flap. There were no significant differences in surgical site infection based on the duration of prophylactic antibiotic use. The operation time, methods of breast surgery, volume of fluid drainage in the first 3 days of the abdominal and breast drains, and day of removal of the abdominal and breast drains did not affect surgical site infection.

**Conclusion:** Based on these data, we do not recommend extending prophylactic antibiotics beyond 24 hours in deep inferior epigastric perforator reconstruction. (*Plast Reconstr Surg Glob Open* 2023; 11:e4833; doi: [10.1097/GOX.0000000000004833](https://doi.org/10.1097/GOX.0000000000004833); Published online 22 February 2023.)

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## INTRODUCTION

An increasing number of patients with breast cancer opt for reconstruction after mastectomy to restore the shape of the breast and limit the potential adverse psychological effects after mastectomy.<sup>1</sup> Breast reconstruction can be performed immediately after surgery [immediate breast reconstruction (IBR)] or later (delayed breast reconstruction), with implant (implant-based breast reconstruction)<sup>2</sup> or flap. IBR offers a native inframammary fold and pliable skin envelope that results in a more natural appearance and limits the psychological impact of surgery. However, IBR is associated with a higher risk of surgical site infection (SSI) when compared with delayed breast reconstruction.<sup>3,4</sup> Infection rates after surgical treatment of breast cancer range from 3% to 15% higher than infection rates after a clean surgical procedure.<sup>5</sup> SSI after IBR is much more common than expected after a clean surgical procedure.

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There are two types of postmastectomy reconstruction: autologous tissue flaps and tissue expanders or implants. Although implant-based breast reconstruction accounts for approximately 80% of postmastectomy reconstructions in the world,<sup>6</sup> autologous tissue has a lower risk of secondary infection and scar contracture. Autologous tissue flaps yield durable and natural outcomes. In Wang's review, 793 of 12,501 (6.3%) IRB procedures were coded for SSI; the combined relative risk of implant loss was 1.17 with less than 24 hours of antibiotics.<sup>5</sup>

Prophylactic antibiotics have been found to be useful in lowering infection rates in other surgical groups; however, there is no consensus on the use of prophylactic antibiotics in breast reconstruction surgery. Previous studies have focused on the effect of the duration of prophylactic antibiotic use on SSI outcomes, particularly in implant reconstruction. We conducted a comparative effectiveness study in patients undergoing immediate deep inferior epigastric perforator (DIEP) flap breast reconstruction to determine the appropriate regimen and duration of prophylactic antibiotics for SSI results.

## METHOD

### Study Design and Participants

This retrospective study included 108 patients who underwent immediate DIEP flap breast reconstruction after unilateral or bilateral mastectomy at Ditmanson Medical Foundation Chia-Yi Christian Hospital between 2012 and 2019. This study was approved by the institutional review board of the Ditmanson Medical Foundation (study approval number: CYCH-IRB No. 2020092) and ClinicalTrials.gov Protocol Registration and Results System (NCT05088239). The patients were divided into three groups according to the duration of prophylactic antibiotic administration. Antibiotics were tapered in stages while monitoring for impact on flap survival and SSI. In the drain group (PAD;  $n = 15$ ), prophylactic cefazolin (1000 mg) was administered 30 minutes before surgery, every 4 hours during the perioperative period, and every 6 hours after surgery for 10–14 days when the drains were removed from the breast and abdomen. In the 3-day prophylactic antibiotic group (PA3;  $n = 11$ ), 1000 mg of prophylactic cefazolin was administered 30 minutes before surgery, every 4 hours in the perioperative period, and every 6 hours thereafter for 3 days. In the 1 day prophylactic antibiotic group (PA1;  $n = 82$ ), patients received 1000 mg of prophylactic cefazolin 30 minutes before surgery, every 4 hours during the perioperative period, and every 6 hours in the postoperative period, and antibiotics were discontinued within 24 hours after surgery. For all patients, the dressings remained in place until the sixth postoperative day. Because it is difficult for patients to record the drainage volume and tube care, we removed the breast or abdominal drainage tube when the daily exudate volume was less than 15 mL, and the patient was discharged. All wounds of breast and abdomen were under occlusion dressing for 1 week in postoperative care. The patients were followed up in the outpatient department

## Takeaways

**Question:** What duration of prophylactic antibiotics use is effective in preventing surgical site infection after breast reconstruction with deep inferior epigastric perforator flap?

**Findings:** The risk of surgical site infection did not vary by duration of prophylactic antibiotics (1 day, 3 days, or >7 days).

**Meaning:** Discontinuing prophylactic antibiotics within 24 hours is sufficient to prevent the occurrence of surgical site infection.

for 1 year. This study was conducted in accordance with PROCESS criteria.

### Data Collection

In this investigation, the characteristics of the patients were age, body mass index (BMI), smoking and neoadjuvant chemotherapy, weight of the DIEP flap, operation time, breast operation methods, first 3 days and total amount of breast and abdominal drainage, days until removal of the breast and abdominal drains, necrosis of the DIEP flap, abdominal wound dehiscence, SSI, and SSI wound culture.

### Statistical Analysis

All analyses were performed using SPSS version 21.0 software package (SPSS Inc, Chicago, Ill.); a  $P$  value less than 0.05 was considered statistically significant. Continuous variables are expressed as mean  $\pm$  SD, and categorical data are expressed as numbers and percentages. Statistical analyses were performed using one-way analysis of variance with Scheffe post-hoc test for continuous variables and Pearson  $\chi^2$  test for categorical variables.

## RESULTS

The patient characteristics are shown in [Table 1](#). Four patients (3.7%; 4/108) were smokers, but they quit 2 weeks before the operation. Eighteen patients (16.67%; 18/108) completed six to eight chemotherapy cycles 4 weeks before the operation because of axillary lymph node or distal metastasis. There were no significant differences ( $P > 0.05$ ) in age, BMI, smoking status, or neoadjuvant chemotherapy between the three groups.

One patient had SSI of the breast (0.93%; 1/108) after half DIEP flap necrosis and secondary infection with oxacillin-resistant *Staphylococcus aureus*. However, there were no significant differences ( $P = 0.852$ ) in the prevalence of SSI between the groups. The groups varied significantly by operation time ( $P = 0.013$ ) and breast operation method ( $P = 0.022$ ), but these differences had no effect on the risk of SSI ([Table 2](#)). There were also significant differences ( $P < 0.001$ ) in the first 3 days and total postoperative abdominal drainage and days of removal of the breast and abdominal drains within the groups; however, this did not influence the risk of SSI ([Table 3](#)).

**Table 1. Patient Characteristics**

	PAD (N = 15)	PA3 (N = 11)	PA1 (N = 82)	P
Age	43.73±8.95	46±8.2	44.74±7.72	0.772
BMI	22.92±2.84	23.92±2.76	23.06±3.5	0.703
Smoking				0.442
No	14 (93.33%)	10 (90.91%)	80 (97.56%)	
Yes	1 (6.67%)	1 (9.09%)	2 (2.44%)	
Neoadjuvant chemotherapy				0.174
No	15 (100.00%)	9 (81.82%)	66 (80.49%)	
Yes	0 (0.00)	2 (18.18%)	16 (19.51%)	

**Table 2. Intraoperative Analysis of Flap Weight, Operation Time and Breast Operation Methods in These Three Groups**

	PAD (N = 15)	PA3 (N = 11)	PA1 (N = 82)	P	Post Hoc
Flap weight (g)	534.6±167.68	528.82±194.73	515.68±213.97	0.937	
Operation time (min)	437±67.37	520.45±96.99	448.44±77.25	0.013	PA3 > PAD; PA3 > PA1
Breast operation				0.022	
MRM	1 (6.67%)	2 (18.18%)	38 (46.34%)		
SS	13 (86.67%)	9 (81.82%)	42 (51.22%)		
Other	1 (6.67%)	0 (0.00)	2 (2.44%)		
SSI				0.852	
No	15 (100.00%)	11 (100.00%)	81 (98.78%)		
Yes	0 (0.00)	0 (0.00)	1 (1.22%)		

MRM, modified radical mastectomy; SS, simple mastectomy plus sentinel lymph node dissection.

**Table 3. Postoperative Analysis of Abdominal and Breast Drainage, Abdominal Wound Dehiscence, and SSI**

	PAD (N = 15)	PA3 (N = 11)	PA1 (N = 82)	P	Post Hoc
First 3 days abdominal drainage (mL)	272±101.98	214.45±104.35	72.96±47.65	<0.001	PAD > PA1; PA3 > PA1
Total abdominal drainage (mL)	483.73±237.05	350.45±213.58	104.06±103.36	<0.001	PAD > PA1; PA3 > PA1
Abdomen drain removal (d)	10.27±2.28	9.64±1.96	5.39±1.63	<0.001	PAD > PA1; PA3 > PA1
First 3 days breast drainage (mL)	212.33±110.67	246.91±88.76	237.2±148.73	0.781	
Total breast drainage (mL)	286.6±163.59	405.55±253.67	333.66±260.3	0.486	
Breast drain removal (d)	8.33±1.18	9.64±3.01	7.2±2.14	0.001	PA3 > PA1
Abdominal wound dehiscence				0.479	
No	15 (100.00%)	10 (90.91%)	79 (96.34%)		
Yes	0 (0.00)	1 (9.09%)	3 (3.66%)		
SSI				0.852	
No	15 (100.00%)	11 (100.00%)	81 (98.78%)		
Yes	0 (0.00)	0 (0.00)	1 (1.22%)		

Two patients exhibited a small area of fat necrosis during postoperative follow-up by ultrasound but did not require further treatment. Four patients had partial dehiscence of the abdominal wound, which was not counted among the SSI patients, as no bacterial growth or local cellulitis was observed. None of the patients had a breast wound dehiscence.

## DISCUSSION

SSI is distinguished into superficial incisional, deep incisional, and organ/space groups.<sup>7</sup> The rate of SSI is strongly associated with the type of surgical wound. The Centers for Disease Control published a guideline in 1985, which classified surgical wounds into clean, clean/contaminated, contaminated, and dirty, reporting an SSI rate of 1% to 5%, 3% to 11%, 10% to 17%, and greater than 27% in these wounds, respectively.<sup>8</sup> The occurrence

of SSI can have an impact on the number of additional operations, tissue or organ loss, the risk of long-term complications, and mortality of the systemic inflammatory response syndrome, and can result in additional medical costs and increased hospital readmissions.

Postdischarge antibiotic prophylaxis is commonly administered after a mastectomy and breast augmentation. Antibiotics are usually prescribed until all surgical drains are removed.<sup>9,10</sup> The American Society of Plastic Surgeons practice guidelines for expander/implant breast reconstruction recommend that, in the absence of surgical drains, antibiotics should be discontinued within 24 hours after surgery. However, when there are drains, the operating surgeon will decide when to stop prophylactic antibiotics.<sup>11</sup> In a survey that interviewed 460 plastic surgeons, 72% of them prescribed outpatient antibiotics after mastectomy with breast reconstruction.<sup>12</sup> In Olsen's study,<sup>13</sup> 5492 of 12,501 (43.9%) mastectomy procedures had prophylactic

antibiotics after discharge in 5 days, and cephalosporins (75.1%) were the most commonly prescribed antibiotics.

According to the World Health Organization Global Guidelines for the Prevention of SSI, prolonged postoperative antibiotic administration reduces the risk of SSI in cardiac, vascular, and orthognathic surgery. Furthermore, these guidelines state that perioperative antibiotic prophylaxis to prevent SSI should not be continued due to the presence of a wound drain, because extended antibiotic usage could lead to the development of resistant organisms and systemic side effects, including severe allergic reactions, pseudomembranous colitis (*Clostridium difficile* infection), and yeast infection.<sup>14,15</sup> In Olsen's study,<sup>13</sup> 0.1% procedures among 12,198 patients had evidence of *Clostridium difficile* infection after mastectomy with or without immediate reconstruction. In contrast, the American Society of Healthcare System Pharmacists and the United States Institute for Healthcare Improvement recommend discontinuation of antibiotic prophylaxis within 24 hours of clean and clean/contaminated surgery. The Centers for Disease Control guidelines for SSI prevention recommend the use of preoperative antibiotic prophylaxis for clean and clean/contaminated surgical procedures, those that involve the implantation of a medical device, or procedures with a high risk of potentially catastrophic SSI.<sup>16</sup>

Breast procedures are classified as clean procedures by the Centers for Disease Control and the Surgical Care Improvement Project; therefore, prophylactic antibiotics should be discontinued within 24 hours after surgery.<sup>16</sup> Mastectomy without immediate reconstruction that fits into this category has reported SSI rates of 3% to 18% in individual studies published in the past decade. This SSI rate is higher than expected after clean procedures.<sup>17</sup> In recent years, some researchers have described breast procedures as "clean-contaminated" procedures due to the presence of the breast microbiome and bacteria in normal breast implants and contamination of breast implants regardless of whether precautions were taken or not.<sup>18,19</sup> In these SSI, there are higher proportions of infections caused by *Staphylococcus aureus*, atypical *Mycobacterium* species, and Gram-negative bacilli than would be expected for this anatomic site.<sup>17,20</sup> Furthermore, prolonged postoperative use of antibiotic cephalosporins did not protect against overall highly virulent infections or implant loss after these SSIs.

IBR with a tissue expander/implant is associated with a higher SSI rate than is delayed breast reconstruction. The average SSI rate after IBR ranges from 5% to as high as 35%.<sup>6,21,22</sup> The unadjusted incidence of SSI in implant reconstruction after mastectomy was 14% with more than 24 hours of antibiotics, 19% with less than 24 hours of antibiotics, and 16% regardless of the duration of the antibiotic. Furthermore, the unadjusted incidences of implant loss were 8% with more than 24 hours of antibiotics, 10% with less than 24 hours of antibiotics, and 9% regardless of antibiotic duration.<sup>5</sup> In Olsen's study,<sup>13</sup> the relative risk in SSI of mastectomy plus implant (2.41), plus flap (2.11), plus flap plus implant (2.17) was greater than the relative risks of SSI in unilateral mastectomy with prophylactic antibiotics after discharge. Patients with a

higher BMI, diabetes, preoperative radiotherapy, postoperative seroma, or wound dehiscence were all more likely to develop SSI during implant reconstruction than patients without these risk factors.<sup>14,23</sup> In Hai's meta-analysis,<sup>24</sup> an overall 5.99% SSI rate was documented in 15,966 mastectomy procedures and IBR, but there is insufficient evidence for the use of extended prophylactic antibiotics after discharge. Therefore, most plastic surgeons prefer to administer extended prophylactic antibiotics after mastectomy with implant reconstruction because of the highly virulent infections and implant loss that occur after SSI.

In autologous tissue reconstructions, SSI occurred in 3.3% of patients who had latissimus dorsi flaps, 6.7% of patients who had pedicle transverse rectus abdominis myocutaneous flaps, 5.9% of patients who had free flaps, and 5.5% of all patients (180/3296).<sup>25</sup> Similarly, in Kim's NSQIP database study,<sup>26</sup> the SSI rates varied by type of flap reconstruction. The SSI rates ranged from 2.8% after pedicle latissimus dorsi flap (with or without concurrent implant), to 5.5% after microvascular free flap, and 6.0% after pedicle transverse rectus abdominis myocutaneous flap. In Wilkins's study,<sup>27</sup> SSI was observed in 4.8% of breast procedures, 3.4% of donor sites, and 8.1% (50/619) of all sites in autologous reconstruction, but higher than 10.0% (162/1615) in implant reconstruction. Flap reconstruction has lower SSI rates than implants because of the limited possibility of foreign body reaction. Flaps fill dead spaces after surgery, and therefore decrease the incidence of seroma or hematoma after mastectomy and provide adequate skin cover that limits the changes in primary wound closure tension. In Masoomi's study<sup>28</sup> (which enrolled 15,211 patients), the overall rate of free flap necrosis was 2.4%. In another study by Unukovych,<sup>29</sup> the prevalence of partial flap loss was 1.2%. In our study, partial or total flaps were strongly associated with SSI after autologous reconstruction. Reducing partial or whole flap necrosis greatly reduces the probability of SSI, which is why we used a bipediced DIEP flap for the breast reconstruction.<sup>30</sup>

The SSI rate at the breast recipient sites after DIEP flap reconstruction was 4.7% to 6.9%<sup>30,31</sup> and at abdominal donor wound was 4.4% (25/571).<sup>32</sup> DIEP flap donor site complications with wound dehiscence (12%–39%), seroma (1%–48%), hematoma (1%–15%), infections (1%–12%), fat necrosis (0%–11%), and umbilical necrosis (2%–3%) significantly affect donor site aesthetics and abdominal wall integrity.<sup>33</sup> Progressive tension sutures, closed drain, use of fibrin sealant, and closed incision negative pressure therapy can decrease postoperative seroma incidence and risk of wound necrosis, thus promoting wound healing. Therefore, these procedures can help reduce the occurrence of SSI in abdominal wounds after DIEP flap harvesting.<sup>34,35</sup>

In Edwards' 480 case study, factors independently associated with SSI were current smoking and advanced age. Diabetes diagnosis, steroid use, high BMI, prior breast surgery, use of neoadjuvant chemotherapy, prior radiation, concomitant axillary surgery, and duration of drainage did not increase SSI rates after mastectomy without reconstruction.<sup>14,36</sup> However, advanced age, diagnosis of hypertension, higher BMI, diagnosis of diabetes



mellitus, American Society of Anesthesiologists score of 3 or 4, previous breast biopsy or surgery, use of neoadjuvant chemoradiation, conservation therapy versus other surgical approaches, presence of hematoma or seroma, excessive intraoperative bleeding, use of a postoperative drain, longer drainage time, and a second drainage tube were significantly associated with an increased risk of SSI. However, other factors such as smoking habit, immediate reconstruction, dissection of the axillary lymph nodes, neoadjuvant chemotherapy, corticosteroid use, and prophylactic antibiotics did not have an effect on the risk of SSI after 681 breast procedures in Xue's meta-analysis.<sup>37</sup> In a separate study, the independent risk factors for SSI were increased BMI, heavy alcohol use, American Society of Anesthesiologists score greater than 2, flap failure, and operative time of 6 hours or more in the study by Nguyen.<sup>38</sup> In our series, the patient's age, BMI, smoking habit, use of neoadjuvant chemotherapy, axillary lymph node dissection, prolonged operation time, and longer drainage time did not affect the risk of SSI after surgery.

In Drury's study<sup>39</sup> (which recruited 1036 patients for flap reconstruction), the SSI rate did not differ between patients who received antibiotics for only 24 hours and those who continued antibiotics beyond the 24-hour postoperative period (5.01% versus 2.92%,  $P = 0.109$ ). Furthermore, duration of antibiotic use was not predictive of SSI in the multivariate regression model. In Liu's study,<sup>40</sup> there was no difference in the overall SSI rate between autologous breast reconstruction in patients who received more than 24 hours of antibiotics (19.5% versus 15.5%;  $P = 0.47$ ). These two studies had higher SSI (>5%) with antibiotics for only 24 hours, but there is no consensus on the use of prophylactic antibiotics for autologous breast reconstruction. With stable surgical technique and high flap success rate and low SSI, gradually reducing the use of antibiotics will not affect flaps and SSI; so we retrospectively analyzed the results of different days of antibiotic use in the three periods. The prevalence of SSI in the breast was 0.93% (1/108), and in the abdomen, it was 0% in our series. These values were lower than those observed after mastectomy alone or after mastectomy with implant reconstruction. The only patient with SSI in our study had breast SSI due to partial flap loss of the bipedicle DIEP flap. We believe that large fat and flap necrosis lead to secondary SSI, and the promotion of the success rate of microsurgical anastomosis is essential. The incidence of SSI was very low and did not vary with the duration of antibiotics or the presence of a drain in the breast or abdominal wall. Prophylactic antibiotics were discontinued within 24 hours after DIEP flap reconstruction, which was sufficient to prevent the occurrence of SSI in our study.

### LIMITATIONS

This study recruited a small number of patients from a single hospital and consisted of being retrospective and patients were not randomly selected in each group. The uneven distribution of patient numbers is due to retrospective statistics that did not increase SSI when antibiotics were phased down. Only one case experienced

SSI, and we could not analyze the risk factors for SSI. Furthermore, none of the patients with diabetes or other comorbidities may have had higher risk factors for SSI and flap failure.

### CONCLUSIONS

Sufficient blood supply to decrease fat or flap necrosis can prevent secondary breast infections. Prolonged antibiotic use did not reduce SSI or flap loss. Based on these data, we do not recommend extending prophylactic antibiotics beyond 24 hours in DIEP flap reconstruction. Patient-centered antibiotic prophylaxis based on a risk assessment model may be a more effective alternative to the current indiscriminate SSI control model.<sup>41</sup>

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