



ORIGINAL ARTICLE

Prolonged antibiotic prophylaxis in tissue reconstruction using autologous fat grafting: Is there a benefit for wound healing?

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Abstract

Fat grafting is a well-established method in plastic surgery. Despite many technical advances, standardised recommendations for the use of prophylactic antibiotics in fat grafting are not available. This retrospective multicentre study aims to analyse the use of prophylactic antibiotics in fat grafting and to compare complication rates for different protocols. A retrospective medical chart review of 340 patients treated with fat grafting of the breast from January 2007 to March 2019 was performed in three plastic surgery centres. Complications, outcomes, and antibiotic regimes were analysed. The Clavien-Dindo classification was applied. All patients received perioperative antibiotic prophylaxis: 33.8% (n = 115) were treated with a single shot (group 1), 66.2% (n = 225) received a prolonged antibiotic scheme (group 2). There was no significant difference in the number of sessions ($P = .475$). The overall complication rate was 21.6% (n = 75), including graft resorption, fat necrosis, infection, and wound healing problems. Complication rates were not significantly different between groups. Risk factors for elevated complication rates in this specific patient group are smoking, chemotherapy, and irradiation therapy. The complication rate for lipografting of the breast is low, and it is not correlated to the antibiotic protocol. The use of prolonged prophylactic antibiotics does not lower the complication rate.

KEYWORDS

antibiotic prophylaxis, fat grafting, lipofilling, tissue reconstruction, wound healing

Key messages

- there are no standardised recommendations available in the literature for the use of prophylactic antibiotics in fat grafting
- the purpose of the study was to analyse the arbitrary use of antibiotic substances in fat grafting procedures and complication rates and to compare different protocols

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- smoking, chemotherapy, and irradiation therapy lead to significantly more complications after fat grafting surgery
- the overall complication rate for lipografting of the breast is low, and it is not correlated to the antibiotic protocol
- the use of prolonged prophylactic antibiotics does not lower the complication rate in fat grafting

1 | INTRODUCTION

Autologous fat grafting is a trending and reliable technique in plastic surgery that profits from many benefits such as low donor-site morbidity, minimal scarring, and high patients' satisfaction,^{1,2} not least of all because of the additional liposuction procedure that is needed to harvest the fat tissue. Apart from use in breast augmentation, lipografting covers a wide panel of indications.³⁻⁹ Although there have been great advances in the technique of lipografting, the largely unpredictable take rate remains a concern, with resorption rates ranging from 30% to 80% documented in the literature.¹⁰ Complication rates for autologous lipografting are considerably low and largely attributable to poor technique, unsuitable recipient bed, and infectious agents,^{11,12} including fat embolisation, infection, the formation of oil cysts after graft necrosis, or wound healing problems.^{13,14} In the breast, the risk for infection might be slightly higher due to the presence of a natural bacterial flora in the milk ducts. Therefore, antibiotics are widely used in the perioperative setting of lipografting of the breast.¹³ Uncritical use of antibiotic substances should be avoided at all times because it contributes to the increasing global burden of drug resistance.¹⁵ However, no distinct guidelines or protocols concerning perioperative antibiotic therapy have been defined in the literature so far despite the recent release of an international expert consensus on fat grafting of the breast.¹⁶ On the other hand, no benefit of prolonged antibiotic prophylaxis was found in recent literature regarding reduction mammoplasty¹⁷ and primary and secondary aesthetic breast surgery,¹⁸ with conflicting data on mamma reconstruction.¹⁹

The aim of this retrospective, multicentre study was to analyse the use of prolonged antibiotic prophylaxis (PAP) in breast lipofilling at three plastic surgery centres. We compared the use of PAP to the use of antibiotic single-shot prophylaxis, analysing the outcomes and complications of the procedure depending on risk factors and the different perioperative antibiotic protocols. In this study, we provide a distinct recommendation for the use of perioperative antibiotics in autologous fat grafting of the breast for the first time in medical literature.

2 | MATERIALS AND METHODS

2.1 | Data acquisition

Data from all patients scheduled for elective fat grafting of the breast during a period of 12 years from January 2007 to March 2019 at the Department of Plastic, Reconstructive and Aesthetic Surgery; the Medical University of Innsbruck (Austria); the Department of Hand, Plastic and Reconstructive and Hand Surgery; St. Gallen Canton Hospital (Switzerland); and the Department of Plastic and Aesthetic, Reconstructive and Hand Surgery, Agaplesion Markus Hospital, Frankfurt am Main (Germany) were reviewed in the electronic medical record database. These data were collected retrospectively. Due to the retrospective character of data acquisition, a waiver of review was granted by the local ethics review board. The authors declare that the ethical guidelines of the 1975 Declaration of Helsinki as amended in 2013 were followed at all times when conducting this work. All patients gave their oral and written informed consent for the procedure and the use of their data and photographs in scientific publications. The STROBE guidelines were followed.²⁰ Due to the concerns raised in the literature by Petit et al in 2011,²¹⁻²³ from that time we pursued the policy of not performing fat grafting of the breast within a time frame of 12 months after treatment of breast cancer. Patients who exclusively underwent isolated lipografting of the breast area were included in the study. Exclusion criteria were as follows: (a) lipografting of the breast performed simultaneously with any other surgical procedure or (b) lipografting of another area of the body. The reviewed data included age, body mass index (BMI), smoking, history of radiation therapy of the recipient site or chemotherapy, allergies, and comorbidities.

2.2 | Antibiotic therapy

The use of perioperative and postoperative intravenous antibiotics and the follow-up history were analysed and recorded. Patients were divided into two groups: the patients in the single-shot group who received one dose

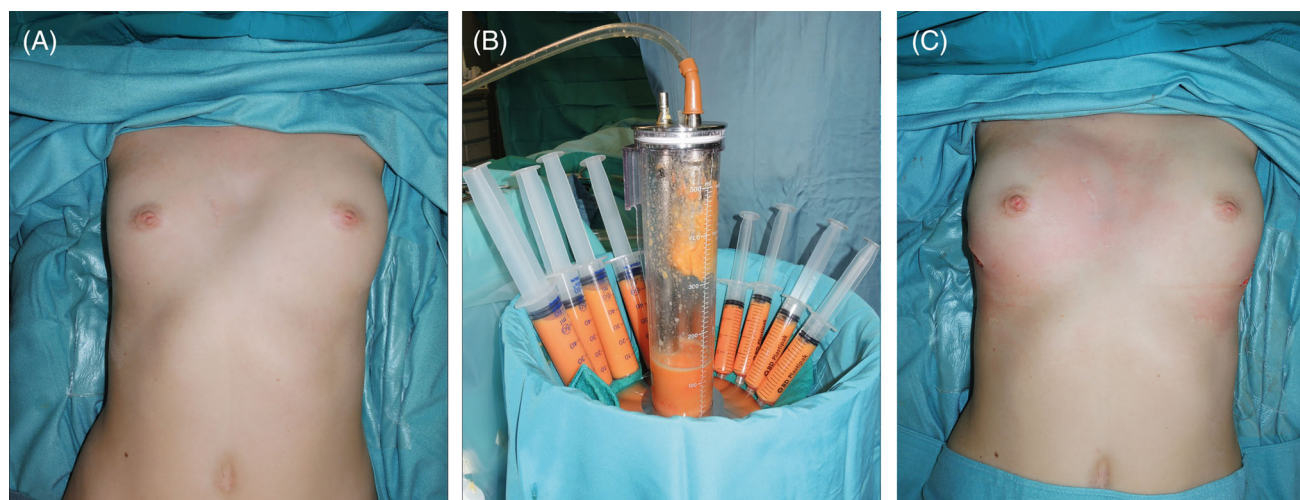


FIGURE 1 Representative perioperative setting for fat grafting of the breast of a 24-year-old female that underwent correction of pectus excavatum with a pectus bar 2 years before. After pectus bar removal, residual breast asymmetry (A) was corrected employing fat grafting. Following harvest, fat tissue is decanted (B) and subsequently transferred to smaller syringes. The postoperative result is shown in C

TABLE 1 Patients characteristics and descriptive statistics

	Mean (%) (range)		Total
	Group		
	Single shot	PAP	
Patients (n)	115 (33.8%)	225 (66.2%)	340 (100%)
Male (n)	12	3	15 (4.4%)
Female (n)	103	222	325 (95.6%)
Age (y)	48 (18-75)	42 (16-69)	42.4 (16-75)
BMI (kg/m ²)	24.2 (15.1-38.2)	23.9 (17.19-39.1)	23.9 (15.1-39.1)
Number of sessions per patient (n)	2 (1-6)	1 (1-7)	1.65 (1-7)
Injected volume in total per session (mL)	242.8 (15-1275)	311.1 (15-1560)	288.2 (15-1560)
Patients with history of irradiation (n)	57	75	132 (38.8%)
Patients with history of chemotherapy (n)	46	56	102 (30%)
Smokers (n)	39	69	108 (31.7%)

Abbreviation: BMI, body mass index.

of the antibiotic prophylaxis at the beginning of the surgical procedure (group 1); the patients in the PAP group who received a prolonged antibiotic prophylaxis (72 hours or more) (group 2). The first dose was intravenous, postoperative doses were administered orally. Standard follow-up visits in the outpatient clinic were conducted at 2 weeks and 3 months postoperatively. Complications such as resorption, the formation of oil cysts, clinically apparent infection, and wound healing problems were documented. Key outcome parameters were analysed for each patient in accordance with the recently released international expert consensus on fat grafting of the breast,¹⁶ documenting the complications

according to the Clavien-Dindo classification,^{24,25} outcome, and the number of fat grafting sessions needed to obtain the optimal result, noting that every single procedure had the aim of reaching the desired volume without follow-up procedures.

2.3 | Surgical technique

Patients were operated under general anaesthesia. Tumescence solution according to Klein^{16,26} or Illoz²⁷ was used for infiltration before fat harvest. After 15 minutes, fat was harvested using the low-pressure pump-assisted

FIGURE 2 Indications for fat grafting to the breast area

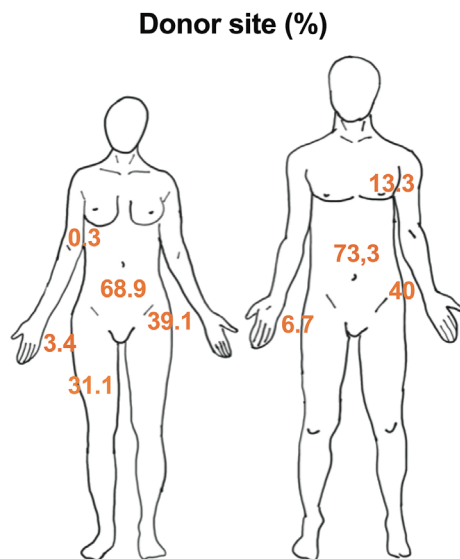
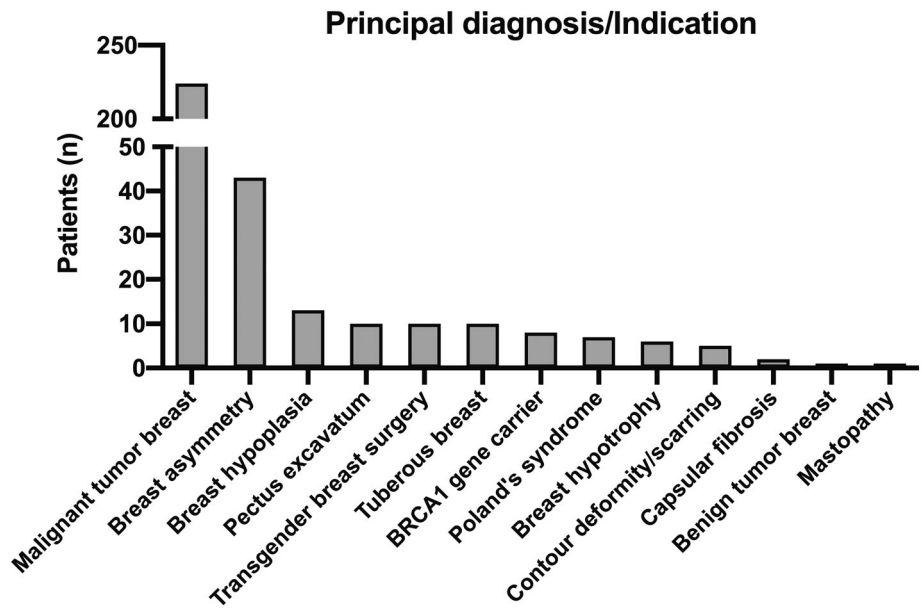


FIGURE 3 Donor sites (%)

system (BodyJet, HumanMed, Germany) with a 5-mm-diameter cannula, collecting the fat in a sterile closed filtration chamber connected to a standard surgical vacuum. This procedure was followed by decantation of the harvested tissue (Figure 1). The decanted fat was then transferred to 5- and 10-mL LuerLock syringes (Terumo Europe N.V. Corporation, Leuven, Belgium) without further processing and was injected with 2- and 3-mm blunt Coleman style cannulas (Tulip Medical Products, San Diego) through multiple passes in the breast tissue in a fan-like injection pattern with slight overcorrection. Restricting scars were treated by rigotomy²⁸ followed by injection of small fat deposits into the released scar area.

2.4 | Statistics

Continuous variables are presented as mean \pm SD with range. Categorical data are presented as the number of cases with percentage. Baseline characteristics between single shot and PAP were tested with unpaired student's *t*-tests for normally distributed continuous variables or Mann-Whitney *U* tests for non-normally distributed continuous variables. For categorical variables, Fisher's exact tests were used. The correlation of patient's characteristics with clinical outcome was modelled with multivariable logistic regression analysis. All analyses were performed with SPSS (Statistical Package for the Social Sciences) version 25 (IBM; Armonk, New York), StatView statistical software (SAS institute Inc., version 5.0.1), and Prism 5 (GraphPad software Inc., version 5.0). *P*-values of .05 or less was considered to indicate statistical significance.

3 | RESULTS

3.1 | Descriptive statistics

In total, 340 patients met the inclusion criteria and were included in the study. Descriptive patients' characteristics are shown in Table 1. All indications for lipografting are summarised in Figure 2. In 224 patients (65.8%), previous surgery due to malignant disease of the breast was found in the medical history. A history of previous breast reconstruction surgery applying autologous or implant-based reconstruction was found in 184 patients (54.1%) after malignant disease of the

TABLE 2 Required number of fat grafting sessions per patient

Sessions (n)	Patients (n)	%
1	210	61.8
2	82	24.1
3	33	9.7
4	8	2.4
5	4	1.2
6	2	0.6
7	1	0.3

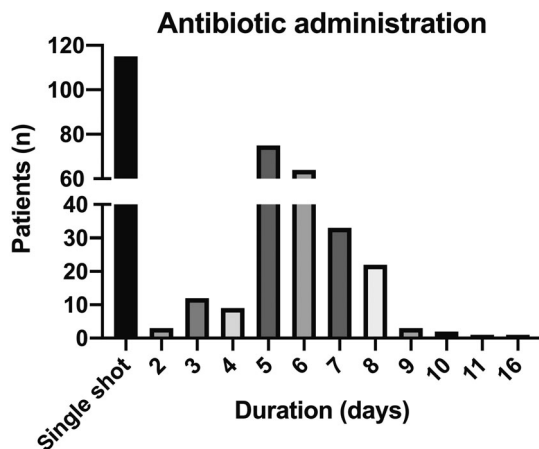


FIGURE 4 Duration of antibiotic administration

breast. In total, 108 patients (31.7%) were active smokers at the time of the fat grafting procedure, while all other patients reported being non-smokers. Concerning other risk factors, 102 patients (30%) had previous chemotherapy, while a total of 132 patients (38.8%) had previous irradiation therapy of the breast area (Table 1). In this study, time from conclusion of irradiation therapy to the first lipofilling session was mean of 34.7 months (range: 5.7-128.9 months). After breast surgery due to malignant disease of the breast tissue, mean time to lipofilling after breast reconstruction was 21.2 months (range: 4-107.7 months).

3.2 | Lipofilling procedure

The most frequently requested and used donor site for fat harvesting was the abdomen. Donor sites are depicted in Figure 3. In more than 50% of patients, more than one donor site was used per session. Mean grafted volume per session was 288.2 mL (range: 15-1560 mL). In total, 210 patients (61.8%) required only one session to reach their personal optimal result, as summarised in Table 2.

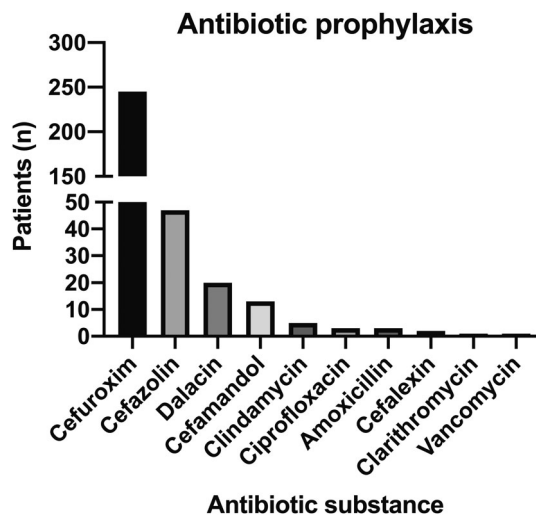


FIGURE 5 Antibiotic substances used for antibiotic prophylaxis in breast lipofilling

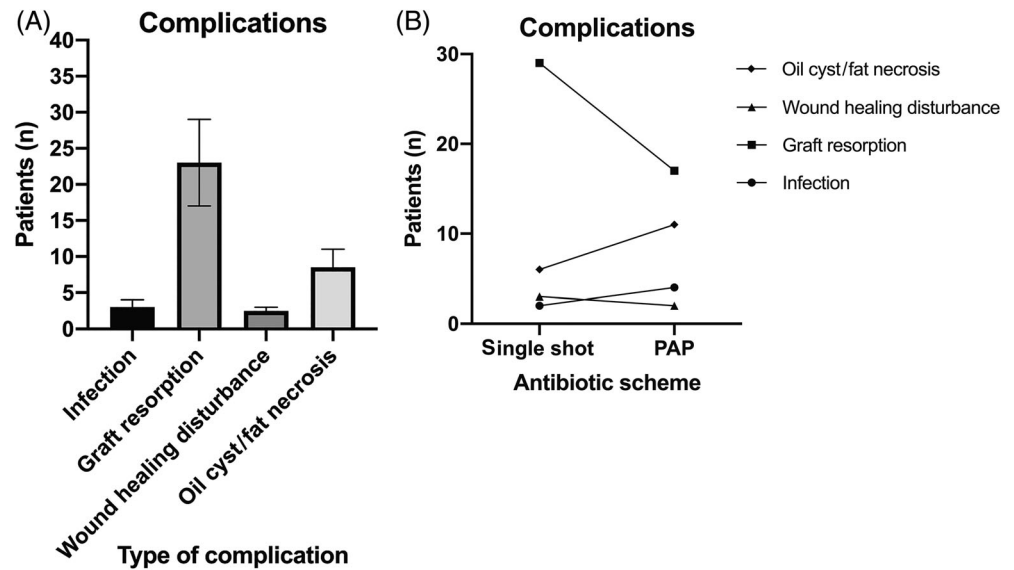
3.3 | Antibiotic prophylaxis

The patients were grouped according to the duration of the antibiotic prophylaxis they received in the perioperative setting. In total, 33.8% (115 patients) received a single-shot antibiotic prophylaxis at the beginning of the procedure (group 1), whereas the other 66.2% ($n = 225$) received a prolonged antibiotic prophylaxis (PAP, group 2) for minimum 72 hours. In the PAP group, most patients received the antibiotic for 5 to 6 days (40.9%), as depicted in Figure 4. The vast majority of patients (85.9%) received second-generation cephalosporins (cefuroxime, 72.1% or cefazolin, 13.8%). If patients reported an allergy against any beta-lactam antibiotic substance (5.9%), clindamycin was used. Other antibiotics were used only sporadically (Figure 5).

3.4 | Complications

In total, 21.6% ($n = 74$) of all patients sustained minor but clinically apparent complications that were recorded during the standard follow-up visits in the outpatient clinic at 2 weeks and 3 months postoperatively. Complications are depicted in Figure 6A. Patients with complications were grouped according to the antibiotic prophylaxis they received in the perioperative setting (single-shot vs PAP), as shown in Figure 6B. In this study, none of the complications were seen significantly more frequently in one of the groups, including fat necrosis with subsequent formation of oil cysts ($P = .528$), clinically evident resorption of the graft ($P = .349$), infection ($P = .679$), and wound healing disturbance ($P = .21$),

FIGURE 6 Complication frequency (A) and correlation with antibiotic prophylaxis group (B)



indicating that in terms of complication rates the prescription of a prophylactic antibiotic for more than 2 days did not provide a benefit as compared to the antibiotic single shot. Also, the number of sessions needed to reach the desired graft volume did not significantly differ between the two groups ($P = .475$), consistent with the matching data on graft resorption.

Frequency of complications was analysed in consideration of the medical history and, herein, patients' individual risk factors. Smoking, previous chemotherapy, or irradiation therapy of the graft site were considered risk factors for impaired outcome. In fact, these patient groups showed significantly more complications in the postoperative clinical course than others. This effect shows to be irrespective of the duration of the antibiotic prophylaxis (single shot vs PAP), indicating that it was instead attributable to the individual risk factor itself, namely smoking ($P = .002$), chemotherapy ($P < .001$), or irradiation of the graft recipient tissues ($P = .014$).

3.5 | Complications according to Clavien-Dindo

In total, 74 patients (21.6%) sustained a clinically apparent complication in the postoperative clinical course. Following the international expert panel consensus on fat grafting of the breast,¹⁶ complications were grouped according to the widely used Clavien-Dindo classification.^{24,25} In 65 cases (19.1%), a class 1 complication was recorded, which includes any deviation from the standard postoperative course such as the administration of antiemetics or fluid management. However, in eight (2.4%) cases, a class 2 complication occurred, including

prolongation of the antibiotic therapy in cases of local infection of the graft site. Clavien-Dindo class 3 was assigned to only one patient (0.3%), thus necessitating the removal of a large fat tissue necrosis in general anaesthesia. No potentially life-threatening or deadly complications (Clavien-Dindo class 4 or 5) were seen in this study.

4 | DISCUSSION

Autologous lipotransfer has proven to be a helpful tool in plastic surgery. Because of the limited take rates after a proposed healing period of 3 months,¹⁰ repeat sessions are often required being a result of poor recipient site tissue quality and patients' personal risk factors such as smoking. Scientific data on how free fat tissue is integrated into the recipient tissue are limited and knowledge on the immediate postoperative phase remains elusive. Nevertheless, it is known that in the early phase, the graft is dependent on diffusion and that plasmatic imbibition helps nourish the graft until it becomes vascularised.²⁹ Rapid vascularisation seems crucial,³⁰ and until then the graft has to be protected from harmful impacts such as mechanical cues or infectious agents. Moreover, anti-apoptotic effects on free fat grafts exerted by certain antibiotic substances have been postulated.³¹ Hence, most surgeons prefer to add antibiotics to their postoperative regime following autologous lipotransfer with the goal of maximising safety of the procedure. Distinct guidelines are lacking so far. As shown in a rather small series by another group,¹³ most surgeons prefer quite different antibiotic regimes. In this multicentre appraisal, we were able to confirm this finding, hypothesising that

this is an effect of concern and lack of evidence. In our opinion, this quite clearly depicts the need for a distinct guideline.

Analysing the different antibiotic agents used for surgical antibiotic prophylaxis throughout the literature, the chosen substances might not always be appropriate.³² In the vast majority of our cases, first-generation cephalosporins were used, preferring the use of clindamycin in the case of a known allergy to beta-lactam antibiotics. In fact, cefuroxime is one of the most frequently used agents for perioperative prophylaxis.³³ Nonetheless, adherence to guidelines issued by local microbiology institutes might be helpful with regard to the ever changing microbial resistance patterns, which will also help to reduce the burden of antibiotic resistance. Interestingly, the recently published international consensus on fat grafting of the breast did not include a recommendation on the use of perioperative antibiotic prophylaxis despite offering 10 key messages to follow.¹⁶ This again clearly demonstrates the lack of evidence and guidelines in the literature.

Although most authors consider smoking³⁴ as well as previous chemotherapy and irradiation of the recipient site³⁵ as limiting factors for autologous lipografting due to an increased complication rate, reports of beneficial effects of fat grafting on irradiated tissue³⁶ keep appearing in the literature. In this work, we found a slightly elevated complication rate not only in postirradiation patients but also in smokers and patients who had previously had chemotherapy. However, this effect was independent of the antibiotic regime that was applied. Contrarily, we can therefore draw the conclusion that the use of antibiotic agents does not seem to rescue the negative effect of poor recipient site tissue quality and impaired vascularisation. This is supported by the fact that the antibiotic substances are distributed via blood vessels, and hence, their effect is somewhat dependent on adequate vascularisation. In general, the complication rates of breast augmentation with autologous fat grafting are remarkably low,³⁶ but seem to be slightly enhanced in patients after adjuvant breast cancer treatment.³⁷

Aiming to analyse the outcome of different antibiotic protocols used in this cohort, we divided the patients into two groups, namely the single-shot group and the PAP group (prolonged antibiotic prophylaxis, antibiotic therapy for minimum 72 hours).³⁸ The complications seen in our patient cohort included local infection, wound healing disturbance, and fat necrosis with subsequent formation of oil cysts or clinically evident graft resorption. The latter gives rise to the need for more fat grafting sessions to achieve the volume desired by the patient. Due to largely

lacking easy-to-apply volumetric options, the number of sessions needed to reach the optimal graft volume seems to be an accepted measure for graft resorption in the literature,¹⁶ bearing in mind that every session of fat grafting performed in this cohort had the aim of reaching the full take of the desired final volume. However, as depicted in Figure 6, none of the different complications showed a significantly higher incidence that was dependent on the antibiotic scheme. Accordingly, there was no significant difference in the number of sessions needed to reach the desired graft volume and the optimal result for each patient. This fact also strongly supports the results concerning graft resorption, which is accepted as an indirect measure of graft take rate in the literature,¹⁶ and moreover depicts patient satisfaction and clinical outcome in one easy to measure parameter.

The limitations of this study are the retrospective character and the fact that not all the procedures were performed by the same plastic surgeon despite using the same standard of treatment.

5 | CONCLUSIONS

Our results show that the complication rate for lipofilling of the breast is quite low and is not correlated to the used antibiotic protocol. Specific risk factors for an elevated complication rate in this specific patient group are smoking, chemotherapy, and irradiation therapy. Our study shows that the use of prophylactic antibiotics other than a single shot does not improve the rate of wound healing problems, infection, oil cyst formation, and graft resorption and might therefore not be necessary. Instead, the use of a simple antibiotic single shot seems feasible and is recommended by our group. Large, prospective studies are needed to confirm the data and establish clinical guidelines.

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CONFLICT OF INTEREST

The authors declare no potential conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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