

ORIGINAL ARTICLE

Cosmetic

Complications following Permanent Filler Injection: A Prospective Cohort Study and Protocol of Management

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Introduction: Permanent filler (PF) substances are increasingly utilized in aesthetic procedures. Concurrently, complications related to fillers have also risen. This study aims to determine the rate of complications secondary to PF injections and develop a therapeutic approach for treating such complications.

Methods: This cohort study was conducted by distributing a checklist form among all patients aged 18 years or older who arrived for a new cosmetic consultation between 2015 and 2019. The primary outcome was the occurrence of complications, which are defined as symptoms induced by the PF. The demographics, type of PF, injection site, the time for the complication to occur, and signs and symptoms were recorded and followed up.

Results: In this study, 325 out of 503 (64.61%) patients presented with PF-related complications. About 92.8% were women. All patients with PF-related complications presented with a lump (n = 325, 100%). In regard to the anatomical area of injection, the most common areas were the cheeks (66.6%). The time it took for the complication to occur most commonly ranged from 1–5 years (39.2%, P < 0.001). Complications were significantly higher among patients who received the injection in a nonmedical facility (P < 0.0002). Seventy-seven cases (15.3%, P < 0.0001) underwent PF removal. **Conclusions:** PF-related complications in the body exhibit a wide range of onset and adverse events. The best method to prevent complications caused by permanent filling materials is to avoid them altogether. When it comes to permanent filling agents, we suggest extreme caution. (*Plast Reconstr Surg Glob Open 2022;10:e4687; doi: 10.1097/GOX.00000000004687; Published online 28 November 2022.*)

INTRODUCTION

Soft-tissue filler injections are the second most common cosmetic procedure in the United States (after Botulinum toxin type A). The number of soft-tissue filler injection interventions has risen significantly, with 3.4 million soft-tissue fillers injected in 2020.¹ Not all fillers are approved for cosmetic usage. Guidelines in Europe and

From the *Division of Plastic Surgery, Department of Surgery, King Saud University Medical City, King Saud University, Riyadh, Saudi Arabia; †Department of Plastic Surgery and Burn Unit, King Saud Medical City, Riyadh, Saudi Arabia; and ‡Plastic Surgery Division, Surgery Department, King Fahad Medical City, Riyadh, Saudi Arabia.

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Copyright © 2022 The Authors. Published by Wolters Kluwer Health, Inc. on behalf of The American Society of Plastic Surgeons. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal. DOI: 10.1097/GOX.00000000004687 the United States vary in numerous ways. The most common indication for such substances is cosmetic rejuvenation. Medical conditions, such as lipoatrophy of the face, are less frequent.² Fillers are categorized as temporary, semipermanent (where the duration is at least 18 months), or permanent fillers (PFs) based on how long they remain in tissue. They may also be categorized based on the content of the product.³ To be approved medically, the ideal filling material would have to fulfill specific criteria, such as being easy to apply, nontoxic, noncarcinogenic, nonimmunogenic, and ensuring an excellent aesthetic result.³ The most commonly used PFs are silicone-based products, polyalkylimide, polyacrylamide, and polymethyl

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Related Digital Media are available in the full-text version of the article on www.PRSGlobalOpen.com. methacrylate.⁴ Although these injections are safe and simple and have become an attractive alternative to cosmetic procedures requiring incision, such as fat grafting or facelift procedures,⁵ their widespread use globally leads to increased complications.⁶ The documented adverse events have increased physician and patient awareness of one of the most severe problems associated with filler injections, such as intravascular complications.⁷

Furthermore, it is critical for injecting practitioners to thoroughly understand the anatomy, vascular risk zones, and potential problems. Correspondingly, they must be alert about needed treatment and ensure that patients get the best care possible.⁸ Even though the incidence of complications secondary to soft-tissue augmentation with PFs has been established internationally,^{5,9–11} the knowledge gap in estimating the rate of complications related to PFs among Saudi patients is lacking. Therefore, this cohort study aimed to estimate the complication rate related to soft-tissue augmentation with PFs among patients presenting to plastic surgery clinics and establish a treatment protocol for treating complicated PFs used for soft-tissue augmentation.

METHODS AND MATERIALS

Study Design and Data Collection

This prospective cohort study was conducted by distributing a checklist constructed with assistance from field experts, among all patients aged 18 years or older who arrived for a new cosmetic consultation between 2015 and 2019 in three different medical centers in Riyadh, Saudi Arabia. Patients who agreed to fill out the checklist were offered a selfadministered form. Participants were informed about the study, and consent was obtained. Patients completed the form in the waiting room before proceeding to their respective clinic appointments. Those who had PF injections elsewhere and presented to the clinic for PF-related concerns or complications and had a minimum follow-up duration of 6 months were included in the analysis.

End Points

The primary outcome was the occurrence of complications, which are defined as symptoms and signs induced by the PF, including lumps, depression, leather effect, granuloma, sinus, pain, migration, translocation, hypersensitivity, intravascular complications, or allergic reactions. We gathered patients' demographics, including age, gender, comorbidities, anatomical areas of injection, the time for the complication to occur, the type of PF injected, and the number of patients operated on. (**See Supplemental Digital Content 1**, which displays end points distributed among patients who arrived for a new cosmetic consultation, http://links.lww.com/PRSGO/C287.)

Ethical Considerations

This study was performed after receiving ethical approval from the research ethics committee at King Saud University Medical City, Riyadh, Saudi Arabia. This investigation adhered to the ethical principles mentioned in the Declaration of Helsinki. The contributions of the patients

Takeaways

Question: What is the rate of complications secondary to permanent filler (PF) injection?

Findings: This prospective cohort study shows that 64.6% of patients had PF-developed complication, and 77 cases (15.3%, P < 0.0001) underwent PF removal.

Meaning: PF-related complications in the body exhibit a wide range of onset and adverse events.

were voluntary, and signed consent to use the images for publication was obtained from the patients.

The Management Algorithm Protocol

Our treatment protocol for managing PFs is as follows: the senior authors (B.A. and T.A.) think all patients injected with PFs must undergo radiological examination by magnetic resonance imaging (MRI). Two factors dictate the nature of the treatment after that: the appearance on MRI and the location of the filler. On the MRI, two distinct appearances may occur: lakes and snowstorms. Lakes are collected with encapsulated fillers, while a snowstorm indicates areas irregularly infiltrated with PFs across the tissue. Treatment protocols differ according to which appearance is present in which location of the body. An open facelift technique with complete filler removal is advised for the face (Fig. 1). The filler's bursa will be found either superficial or deep. If the bursa is superficial, excision is not recommended as it may adversely affect the blood supply to the facelift flap. However, if deep, it can be cauterized and burned to make it a rough surface, then fat grafted after 3 months. (See Video [online], which demonstrates our technique of removing PFs from the face.) The principle of the method can be applied to any



Fig. 1. Intraoperative characteristics during an open facelift technique were noticed in patients with permanent filler, showing areas of permanent filler were replaced by fibrosis. In addition, the ligament is obliterated by fibrosis and subclinical infection.

other anatomical region in the body where PFs have previously been injected. Figure 2 shows the images of some patients who developed complications following PF injections. PFs in other body locations, such as the hands and buttocks, should also be managed initially by obtaining an MRI of the area. If the MRI shows a lake appearance, an open approach is advised along with burning the bursa or complete excision to normal tissue margins, such as the buttocks area. If, however, the MRI shows a snowstorm appearance, then liposuction and the use of a spatulated cannula to scar the site are followed by a fat graft after 3 months. Figure 3 shows an algorithm for managing PF complications based on the author's experience.

Statistical Analysis

The analysis was performed by RStudio (R version 4.1.1). Categorical variables were presented as frequencies and percentages, whereas numerical variables were expressed as means \pm standard deviation (SD). The proportion of patients with complications was assessed using the one-sample proportion test with continuity correction. Factors associated with complications were explored using a Wilcoxon rank sum test for numerical variables and Pearson's chi-squared test or Fisher exact test for categorical variables. Statistical significance was considered at a *P* value less than 0.05.

RESULTS

Demographic and Clinical Characteristics of Patients

Data extracted from 503 patients were analyzed in the current study. The mean \pm SD age of patients was 34.8 ± 9.4 (ranging from 18 to 68 years old), and the majority of them were women (92.8%). The most commonly presenting

symptoms were lumps (64.6%) and depression (58.1%). In this study, the total number of patients who had complications related to PF was 325 out of 503 (64.61%). The time it took for the complication to occur most commonly ranged from 1 to 5 years (n = 197, 39.2%), less than 1 year (n = 87, 17.3%), followed by 6–10 years (n = 41, 12.61%). The overall survey response rate among the participants was 60.3%. There were no significant differences between participants with and without complications in terms of age and gender. However, the proportions of patients with complications who presented with the following symptoms were significantly higher than those without complications: lumps (76% versus 43.8%, respectively, P < 0.001), depression (76.9% versus 23.6%, respectively, P < 0.001), sinus (8% versus 2.2%, respectively, P = 0.005), pain (25.2% versus 0.0%, respectively, P < 0.001), and hypersensitivity (6.5% versus 0.0%, respectively, P < 0.001; Table 1).

Characteristics of Filler Injections and Surgical Treatment

In general, the cheek was the most common site of injection (66.6%), followed by the eyelids (15.9%) and the hands (7.2%). A great proportion of patients (76.3%) did not know the type of PF received, whereas 6% of them indicated that they received polyalkylimide injections. Almost three-quarters of patients (75.3%) were unsure about the type of medical facility at which they had received the filler injection (medical or nonmedical), while the remaining patients had received the injection in a nonmedical facility. Concerning surgical treatment, the senior surgeons (B.A. and T.A.) operated on 77 cases (23.69%) to remove the PF. Regarding the factors associated with complications, the anatomical areas of injection and the types of



Fig. 2. Images of some of the patients who developed complications following permanent filler injections at different locations. A, Buttocks. B, Dorsum of hand. C–D, Cheeks.



Fig. 3. An algorithm for managing permanent filler based on MRI findings or the location of injected permanent filler according to the author's experience.

Parameter	Category	Overall, N = 503	Complications			
			Yes, N = 325	No, N = 178	Р	
Age	Mean ± SD	34.8 ± 9.4	34.3 ± 9.1	35.2 ± 9.6	0.174	
Gender (%)	Male	36 (7.2)	21(6.5)	15 (8.4)	0.259	
	Female	467 (92.8)	304 (93.5)	163 (91.6)		
Presenting symptoms (%)	Lumps	325 (64.6)	247 (76)	78 (43.8)	< 0.001	
	Depression	292 (58)	250 (76.9)	42 (23.6)	< 0.001	
	Leather effect	162 (32.2)	104 (32)	58 (32.6)	0.485	
	Granuloma	96 (19.1)	64 (19.7)	32 (18)	0.366	
	Sinus	30 (6.0)	26 (8)	4(2.2)	0.005	
	Pain	82 (16.3)	82 (25.2)	0 (0.0)	< 0.001	
	Migration	17 (3.4)	13 (4)	4 (2.2)	0.220	
	Translocation	4(0.8)	4 (1.2)	0 (0.0)	0.173	
	Hypersensitivity	21(4.2)	21(6.5)	0(0.0)	< 0.001	

Boldface values are significant at p < 0.05 level.

fillers were not significantly associated with the incidence of complications. However, a significantly higher proportion of patients who had received their injections in a nonmedical facility developed complications (28.9%) compared to 16.9% who did not develop complications (<0.002). In addition, 15.3% of patients with complications had undergone surgeries compared to 0% among those without complications, and the difference was statistically significant (P < 0.001; Table 2). Furthermore, there was a statistically significant relationship between the time it took for the complication to occur and its incidence, with a P value of less than 0.001.

DISCUSSION

Injections of soft-tissue fillers are the second most common cosmetic procedure in the United States (after Botulinum toxin type A). In 2020, 3.4 million soft-tissue fillers were injected, a significant increase from 2010.¹ The most common types of PFs are silicones, polyalkylimides, polyacrylamides, and polymethyl methacrylates.⁴ The incidence of complications associated with soft-tissue augmentation using PFs has been demonstrated in the literature.^{5,9} In Saudi Arabia, there is a knowledge gap in estimating the incidence of complications related to PFs. As a result, this cohort study assessed the complication rate associated with PF soft-tissue augmentation among patients presenting to plastic surgery clinics and developed a treatment protocol to treat complicated PFs used for soft-tissue augmentation.

In the current study, 64.61% of 503 patients had complications related to PF, which occurred most commonly 1–5 years after the injection. The majority present with lumps (64.6%), followed by a depression over the skin (5%). With regard to the injection site, we found that the cheek is the most common site, and that patients were often uncertain about the medical facility where they received the PF injection, which was significantly associated with an increased risk of complications. Also, there was a statistically significant relationship between the time it took for the complication to occur and its incidence.

Several studies since then have proposed that mild trauma or low-grade infections may elicit a delayed pathogenic immune response.¹²⁻¹⁶ This might explain why our

			Complications		
Parameter	Category	Overall, N = 503 (%)	No, N = 178 (%)	Yes, N = 325 (%)	Р
Anatomical area of injection	Breast	8 (1.6)	4 (2.2)	4 (1.2)	0.734
5	Cheek	335 (66.6)	116(65.2)	219(67.4)	0.725
	Eyelid	80 (15.9)	32 (18)	48 (14.8)	0.949
	Hands	36 (7.2)	13 (7.3)	23 (7.1)	0.647
	Buttocks	26 (5.2)	9(5.1)	17 (5.2)	0.931
	Labia	2(0.4)	0(0.0)	2(0.6)	0.205
	Forehead	2(0.4)	0(0.0)	2(0.4)	0.205
	Nose	4 (0.8)	1(0.5)	3 (0.9)	0.333
	Leg	3 (0.6)	2(0.7)	1 (0.4)	>0.999
	Chin	5 (1.0)	2(1.1)	3 (0.9)	0.663
	Penis	2(0.4)	1(0.4)	1(0.4)	>0.999
Received injection in a nonmedical facility	Do not know	379 (75.3)	148 (83.1)	231 (71.8)	< 0.002
5 /	Yes	124 (24.7)	30 (16.9)	94 (28.9)	
Type of permanent filler injected	Do not know	461 (91.7)	163 (91.6)	298 (91.7)	0.574
71 1 5	Polyalkylimide	30 (6)	10 (5.6)	20 (6.2)	
	Polyacrylamide	8 (2.2)	4 (1.2)	4 (1.8)	
	Silicone	4 (0.8)	1(0.2)	3 (0.6)	
Underwent surgery	Yes	77 (15.3)	0 (0.0)	77 (15.3)	< 0.001
Time it took for the complication to occur	<1 year	87 (17.3)	0 (0.0)	87 (26.8)	< 0.001
1	1–5 years	197 (39.2)	0(0.0)	197 (60.6)	
	6–10 years	41 (12.6)	0(0.0)	41 (12.6)	
	No complication	n 178 (35.4)	178 (100)	0(0.0)	

Table 2. Characteristics of Filler Injections and Surgical Treatment

Values in boldface are significant at p < 0.05 level.

study found such a wide range of onset times for symptoms. Years to decades after injection, granulomatous responses to the PFs have been observed.¹⁷⁻²⁰ Complications with different PFs have also been observed to have a significant range in start time.¹⁰ Nodules can come from a variety of places. They can be caused by a granulomatous response to the PF depot, inappropriate placement of PF material, muscle-induced displacement, capsular contraction, or a granulomatous reaction to the PF depot.^{11,21} The findings are in agreement with our study, as all patients with PF-related complications presented with a lump (100%). All PF materials cause an inflammatory response and the creation of a fibrous capsule after injection.^{11,22} Figure 1 shows the complications among some of the included patients. It is unclear what causes the formation of foreign body granulomas. According to some authors, all granulomatous responses to PFs are considered delayedtype hypersensitivity reactions.²³ The intrinsic features of the injected PF material dictate the type of complication. According to our study, the most common type of PF injected was polyalkylimide. A study conducted by Carella et al²² found that 3 months to 35 years is the time range after the first PF injection for the signs and symptoms to appear. In our study, the timeline for complications caused by PFs showed that 60.71% of patients were expected to suffer some complications 1-5 years after injection. This proves the theory of continued inflammation with time after PF injection. We believe that complications range from 5% to 10% after 6–12 months from the injection, 25%–50% after 5 years, and up to a 75%-100% complication rate after 10 years. There is a high prevalence of complications associated with PF usage, and complications were statistically significant among patients who had their PF injected in a nonmedical facility. In addition, the complication rate increases with the length of time between injections, the longer the period, the higher the complication rate. These correlations need to be confirmed in prospective randomized controlled trials. The most common types of PFs injected among our patients were polyalkylimide and polyacrylamide, followed by polymethylmethacrylate (silicone gel). This finding is consistent with a study conducted in the Netherlands among 85 patients with delayed-onset complications after facial injections with PF, which showed that polyalkylimide was the most commonly used with the highest incidence of complications, polyacrylamide, followed by polymethylmethacrylate.²⁴ Regarding silicone gel, it was widely used in the past century; it became popular, though it was associated with many significant adverse effects. Therefore, it was banned in Europe and the United States of America.^{25,26} In addition, 124 patients injected with PFs were not injected in medical facilities. This leads to higher infection rates and granuloma formation.¹⁷ This also alerts us to a significant issue of supplying medical PFs by nonmedical professionals, which highlights a considerable need for patients to be educated about PFs and their complications. PF complications might be inflammatory or noninflammatory. For years, the word granuloma has been used interchangeably to describe both inflammatory and noninflammatory instances,⁵ whereas other writers believe that hyaluronic acid implants cannot cause granulomatous responses.^{10,27} The type of the injected substance, its injection pattern, and the clinical indications of the problem all play a role in determining the safest and most successful way to remove it.8 Many techniques have been used to manage PF complications and granulomas, ranging from surgical removal to liposuction and removal under ultrasound guidance.^{28,29} Although our sample size was considerable, investigations with bigger patient groups are needed to further study this problem. In addition, we highly encourage future studies to list the complications as symptoms and the main presenting complaints. Despite these flaws, our study design matches real-world clinical practice, and the findings provide valuable information that might help patients.

CONCLUSIONS

There is no consistency in handling PF complications and presentations in the literature. Hence, traditional medical and surgical treatments have failed to meet expectations. This research study demonstrated our experience managing PF complications and presented data from patients who had such complications. Hence, we concluded that PF-related complications in the body exhibit a wide range of onset and types of adverse events. The intrinsic properties of the injected PF might have a role in the observed variation. Finally, we agree with Duffy that the best method to prevent complications caused by permanent filling materials is to avoid them altogether.¹² When it comes to permanent filling agents, we suggest extreme caution.

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