



Which Dermal Filler is Better for Penile Augmentation for Aesthetic Purposes? A Prospective, Single-Surgeon Study Based on Real-World Experience

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Purpose: Several types of dermal fillers have been recently introduced and used for penile augmentation (PA). However, few studies have compared outcomes after the injection of different fillers. This study aimed to compare the clinical outcomes of hyaluronic acid (HLA), polylactic acid (PLA), and polymethyl methacrylate (PMA) filler injections, which are the most commonly used for aesthetic purposes.

Materials and Methods: This prospective study was conducted for 24 weeks after a filler injection by a surgeon between March 2017 and December 2021. Healthy adult men complaining of small penis were enrolled. Penile girth, satisfaction, and injection-associated adverse events (AEs) were assessed at baseline and 4, 12, and 24 weeks after injection.

Results: Of the 301 men who received filler injections, 125, 134, and 42 received HLA, PLA, and PMA fillers, respectively. The augmentation effect was in the order of PMA, HLA, and PLA, respectively, at 24 weeks (PMA vs. HLA, $p < 0.001$; HLA vs. PLA, $p = 0.006$). Satisfaction levels increased significantly at 24 weeks in all groups (each with $p < 0.001$). However, the increase in satisfaction levels was smaller in the PMA group (PMA vs. HLA or PLA, $p < 0.05$, for both penile appearance and sexual life). No serious or systemic AEs were recorded. Filler injection-associated local AEs in the HLA, PLA, and PMA groups occurred in 9 (7.2%), 16 (11.9%), and 6 (14.3%) men, respectively. There was no significant difference in AEs among the groups ($p = 0.299$).

Conclusions: The augmentative effect was greater in the PMA group than in the HLA and PLA groups, whereas the increase in satisfaction levels was smaller in the PMA group. Our study demonstrated the clinical course of different types of fillers and suggests that the filler type should be selected after detailed counseling considering individual characteristics and preferences.

Keywords: Dermal fillers; Hyaluronic acid; Men; Penis; Polylactic acid; Polymethyl methacrylate

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INTRODUCTION

The trend towards safer, less invasive, and more effective treatments has become commonplace in modern medicine. This is especially true in the field of aesthetic medicine because almost all aesthetic procedures are performed according to the patient's desire, not medical necessity [1,2]. In line with this trend, dermal filler injections have surpassed conventional surgical procedures and have become mainstream for soft tissue augmentation. In 2022, dermal fillers were the second most common minimally invasive aesthetic procedure, with approximately 5.7 million procedures, and were performed approximately 3.8 times more than all surgical aesthetic procedures in the United States [3].

As with other aesthetic procedures, penile augmentation (PA) is performed according to the patient's needs in most cases; therefore, the physician must have a clear understanding of the characteristics of the filler injection. However, scientific evidence on the characteristics of filler injections for PA is lacking. Although there is ample evidence of the clinical utility of filler injections into the face, the anatomical structure and physiological functions of the penis are markedly different from those of the face [4,5]. Therefore, it cannot be concluded that the clinical utility of fillers in the penis is similar to that in the face [6].

Several types of fillers have been used, including hyaluronic acid (HLA), polylactic acid (PLA), polymethyl methacrylate (PMA), collagen, and silicone [4]. However, an ideal filler for PA has not yet been developed, and different types of fillers have different clinical properties in terms of injection technique, longevity, removal method, and so on. Therefore, physicians and patients should fully understand the advantages and disadvantages of the different types of fillers available when discussing which type of filler to use. Nevertheless, to the best of our knowledge, only four studies have compared the postinjection clinical course of fillers, and all of them only compared HLA and PLA [6-9]. Furthermore, determining whether previous studies reflected actual clinical practice properly is difficult because they were conducted in a controlled environment to investigate the characteristics of the fillers themselves and did not necessarily reflect the needs of patients.

Among the fillers introduced for PA, the most commonly used fillers clinically are HLA, PLA, and PMA;

these have all been approved for clinical use in several countries [7,10-12]. They possess distinct biochemical and clinical characteristics [4,12]. HLA is a temporary biological filler with passive and direct effects. PLA is also a temporary filler but is a biodegradable synthetic filler with biostimulatory and delayed effects. However, PMA is a permanent synthetic filler material.

Our study aimed to compare the clinical outcomes of HLA, PLA, and PMA fillers for PA 24 weeks postinjection based on real-world experience.

MATERIALS AND METHODS

1. Ethics statement

This study was approved by the institutional ethics committee of Hallym University Chuncheon Sacred Heart Hospital (Reg. No. CHUNCHEON 2024-04-003). The study design, characteristics of each filler, and possible filler-related adverse events (AEs) were explained in detail to each patient. Prior to the filler injection, all patients signed a consent form.

2. Study design

Our prospective, single-center, open-label, single-injection comparative study consisted of a 24-week postinjection period. The 24-week postinjection period was decided, based on the results of previous studies which demonstrated that the augmentative effect of all three fillers stabilized within at least 24 weeks [4,6-9,11,12]. We included patients who visited our hospital to undergo PA using fillers for aesthetic purposes between March 2017 and December 2021.

Each patient chose the desired filler after a counseling session with the physician about the characteristics of each filler and possible filler-related AEs; the options were HLA, PLA, and PMA fillers.

Filler injections and all assessments were performed by an experienced physician. Penile girth and satisfaction with penile appearance were assessed immediately before injection and at 4, 12, and 24 weeks postinjection. Satisfaction with sexual life was assessed immediately before injection and at 12 and 24 weeks. All AEs were reported at 4, 12, and 24 weeks postinjection or immediately upon occurrence.

Penile girth was measured using the method described in previous studies [7,10]. In summary, measurements were performed in a flaccid penile state without stretching, in the supine position. Penile girth

was measured using a measuring tape at the distal shaft (just below the glans), mid-shaft (middle between the proximal and distal shafts), and proximal shaft (just above the penoabdominal junction). The mean penile girth was recorded as the mean of the girth measurements of the distal, mid-, and proximal shafts.

Satisfaction with penile appearance and sexual life was assessed using a 5-point visual analog scale (VAS) ranging from 1 (very dissatisfied) to 5 (very satisfied).

3. Patients

The participants were adult men aged >20 years. Filler injections were not performed in patients with any psychological illness or history, uncontrolled major systemic diseases, coagulopathy, anticoagulant use, or penile malformations. History of penile surgery, including PA, was also an exclusion criterion. Although the uncircumcised penis itself was not a contraindication for filler injection, the patient with severe phimosis received filler injection after circumcision. The baseline characteristics of the patients were described in Table 1.

4. Filler types

The three fillers used in our study have been ap-

proved for PA in Korea and are commercially available in several countries.

The HLA filler (GuguFill; Hanmi Pharm. Co., Ltd.) is a monophasic gel consisting 20 mg of HLA cross-linked by 1,4-butanediol diglycidyl ether ($\geq 95.0\%$) 1.9 μL in 1 mL. The PLA filler (PowerFill; REGEN Biotech Inc.) is a powder consisting 10 g of 50 μm microparticles of PLA suspended in 3 g of 3% carboxymethylcellulose and methylcellulose. It was mixed with 3 g in 7 mL sterile saline immediately before injection. The PMA filler (Lipen; Chunghwa Medipower Co., Ltd.) is a gel consisting 7.5 g of cross-linked dextran, 1.5 g of PMA, and 1 mL of hypromellose solution in 10 mL.

5. Injection method

All injections were performed by an experienced physician. The detailed method has been described previously [7] and is summarized as follows. The injection was performed in an office setting; penile block was achieved with an injection of lidocaine (2% Lidocaine HCL Hydrate Injection; Huons, Co., Ltd.). On the penile base at 2 points (1–2 and 10–11 o'clock positions), an 18-gauge needle was inserted between the Dartos and Buck's fascia. Fanning and multiple puncture tech-

Table 1. Baseline clinical characteristics of patients

Variable	All (n=301)	HLA group (n=125)	PLA group (n=134)	PMA group (n=42)	p-value
Age (y)	43.8±8.0	43.3±8.1	44.5±8.0	43.1±8.0	0.360 ^a
Diabetes mellitus	24 (8.0)	12 (9.6)	9 (6.7)	3 (7.1)	0.678 ^b
Hypertension	35 (11.6)	16 (12.8)	14 (10.4)	5 (11.9)	0.839 ^b
Dyslipidemia	32 (10.6)	13 (10.4)	18 (13.4)	1 (2.4)	0.127 ^b
Erectile dysfunction	21 (7.0)	6 (4.8)	9 (6.7)	2 (4.8)	0.772 ^b
Premature ejaculation	15 (5.0)	6 (4.8)	8 (6.0)	1 (2.4)	0.642 ^b
Circumcision	287 (95.3)	119 (95.2)	129 (96.3)	39 (92.9)	0.654 ^b
Penile girth (cm)					
Mean ^c	8.2±1.1	8.2±1.2	8.2±1.1	8.1±0.8	0.800 ^a
Distal shaft	8.0±1.0	8.0±1.2	8.0±1.0	8.0±0.8	0.980 ^a
Mid-shaft	8.3±1.2	8.3±1.5	8.2±1.1	8.1±0.8	0.513 ^a
Proximal shaft	8.3±1.3	8.4±1.4	8.3±1.3	8.2±0.8	0.850 ^a
Penile length (cm)	6.5±1.8	6.4±1.8	6.6±1.9	6.3±1.8	0.493 ^a
Satisfaction level ^d					
Penile appearance	2.3±0.8	2.2±0.8	2.3±0.9	2.3±0.6	0.888 ^a
Sexual life	2.6±0.7	2.6±0.7	2.7±0.8	2.5±0.5	0.297 ^a
Injected filler volume (mL)	19.4±1.8	18.7±1.7	19.8±1.7	19.9±1.7	<0.001

Values are presented as mean±standard deviation or number (%).

HLA: hyaluronic acid, PLA: polylactic acid, PMA: polymethyl methacrylate.

^aAnalysis of variance test. ^bPearson's chi-square test. ^cThe mean penile girth was defined as the mean of the circumference measures on distal, mid-, and proximal shafts. ^dSatisfactions were assessed with a 5-point visual analog scale, with 1 indicating very dissatisfied and 5 indicating very satisfied.

niques (if necessary) were used during injection. Depending on the penile size and physician's experience, approximately 15 to 20 mL of the filler was injected. Postinjection, the patient wore an elastic penile support bandage for 1 day, was administered antibiotics and nonsteroidal anti-inflammatory drugs for 3 days, and abstained from masturbation or sexual intercourse for 1 month.

6. Statistical analyses

The clinical characteristics of the patients according to the filler type were compared using analysis of variance for continuous variables and Pearson's chi-square test for categorical variables.

Changes in penile girth and satisfaction level within the groups were assessed using a paired t-test and repeated measures analysis of variance with Bonferroni correction. Comparisons of penile girth between the groups were assessed using injected filler volume and baseline penile girth-adjusted analysis of covariance. Comparisons of satisfaction levels between groups were assessed using baseline satisfaction level, penile girth, and change in girth-adjusted analysis of covariance. Missing outcome data were calculated using the last post-baseline observation performed using the forward approach.

All statistical analyses were performed using IBM SPSS Statistics for Windows (version 26.0; IBM Corp.). Two-sided p-values were used for all analyses, and statistical significance was set at $p < 0.05$.

RESULTS

1. Patient characteristics

Overall, 306 patients received the filler injections, of whom 5 did not consent to participate in this study. Among the 301 patients included, 125 (41.5%), 134 (44.5%), and 42 (14.0%) patients selected HLA, PLA, and PMA fillers, respectively. Eleven patients were lost to follow-up.

Table 1 shows the baseline characteristics of the patients. There were no significant differences in any of the variables ($p > 0.05$) except for the injected filler volume ($p < 0.001$).

2. HLA filler

At 24 weeks, an increase in penile girth was confirmed with the naked eye (Fig. 1). The penis appeared natural, without nodules or deformities, and the filler material was soft and pliable.

The mean penile girth increased to a maximum at 4 weeks (2.6 ± 0.1 cm increase, $p < 0.001$) and then gradu-

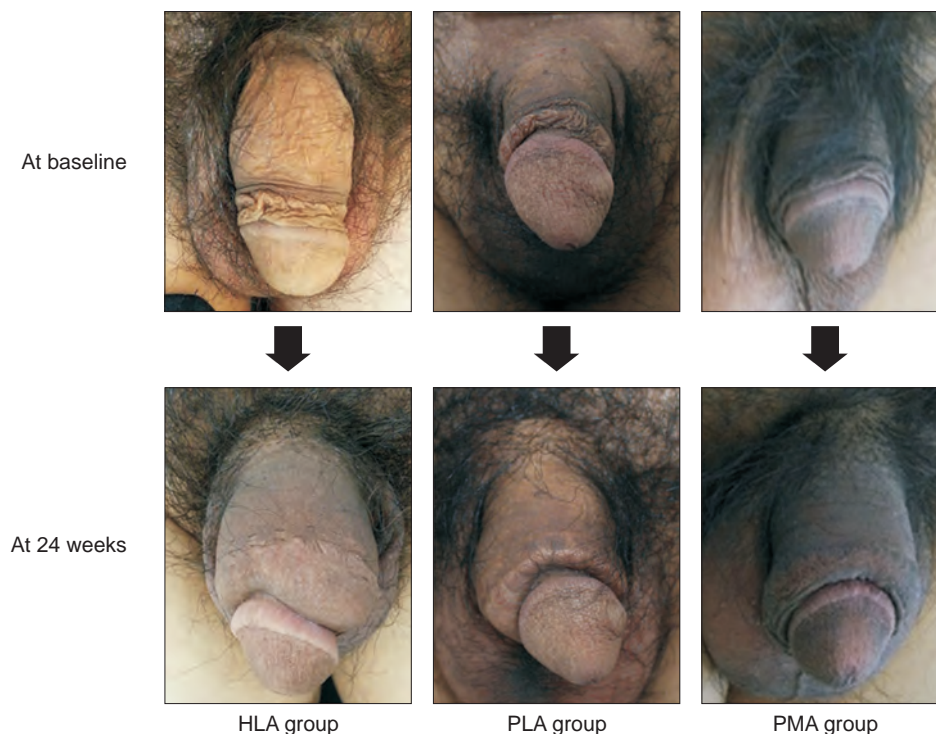


Fig. 1. Representative photos of penis before and after injections of fillers: (A) HLA group, (B) PLA group, (C) PMA group. HLA: hyaluronic acid, PLA: polylactic acid, PMA: polymethyl methacrylate.

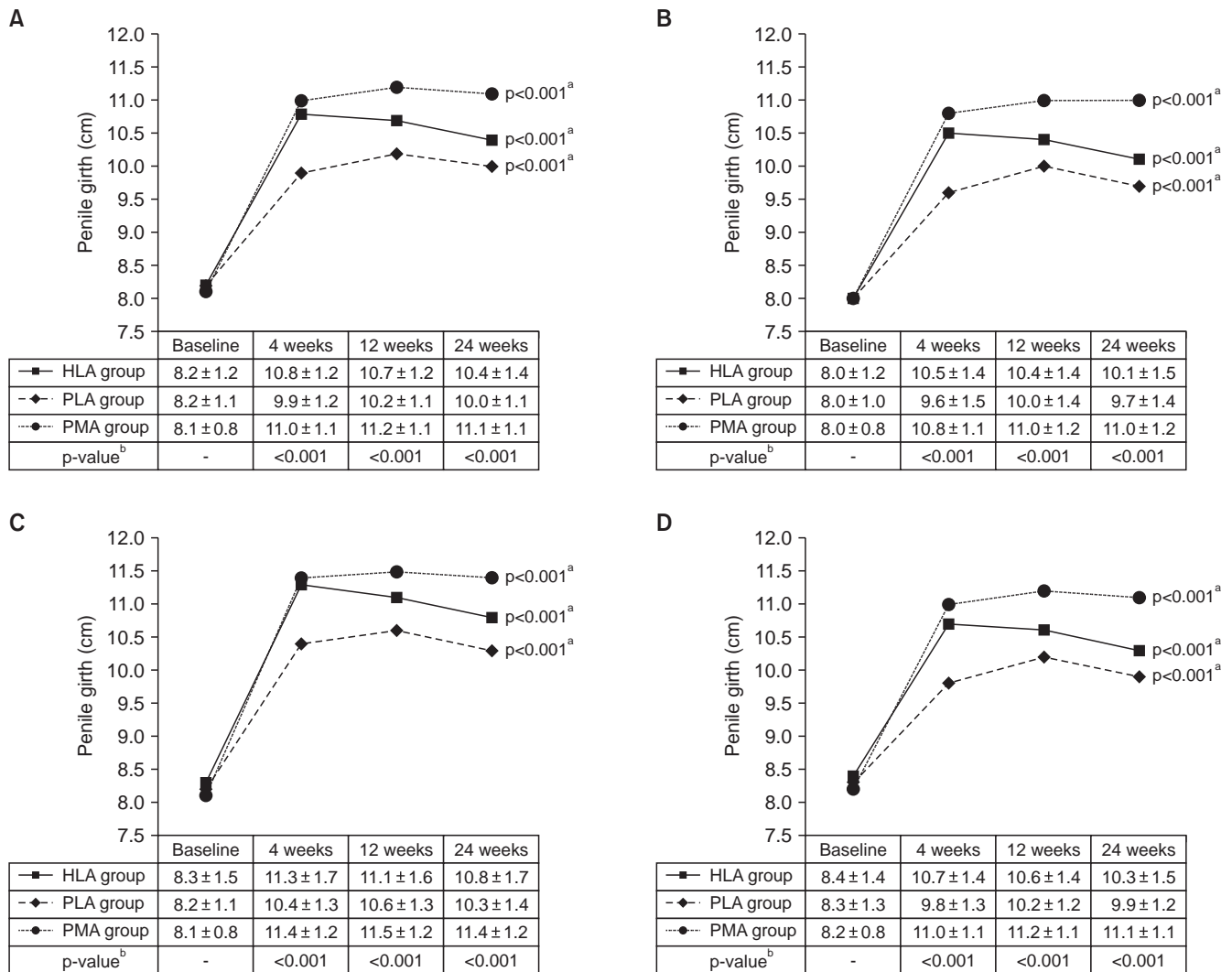


Fig. 2. Changes of penile girth before and after injections of fillers: (A) mean penile girth, (B) distal shaft, (C) mid-shaft, (D) proximal shaft. The mean penile girth was defined as the mean of the circumference measures on distal, mid-, and proximal shafts. HLA: hyaluronic acid, PLA: poly-lactic acid, PMA: polymethyl methacrylate. ^aPaired t-test from base to 24 weeks. ^bInjected filler volume and baseline penile girth-adjusted analysis of covariance test from baseline.

ally decreased till 24 weeks (0.5±0.1 cm decrease from 4 to 24 weeks, $p < 0.001$; Fig. 2A). The trend in the mean penile girth was similar to those in the penile girths measured at the distal, mid, and proximal shafts (Fig. 2B–2D).

The mean VAS score for satisfaction with penile appearance increased to a maximum at 4 weeks (1.4±0.1 score increase, $p < 0.001$) and lasted till 24 weeks (0.1±0.1 score change from 4–24 weeks, $p = 0.359$; Fig. 3A). The mean VAS score for satisfaction with sexual life increased to a maximum at 12 weeks (1.0±0.1 score increase, $p < 0.001$) and lasted till 24 weeks (0.0±0.1 score change from 12–24 weeks, $p = 0.783$; Fig. 3B).

3. PLA filler

At 24 weeks, an increase in penile girth was confirmed with the naked eye (Fig. 1). The penis appeared natural, without nodules or deformities, and the filler material was firm and pliable.

The mean penile girth increased to a maximum at 12 weeks (2.1±0.1 cm increase, $p < 0.001$) and then gradually decreased till 24 weeks (0.3±0.1 cm decrease from 12 to 24 weeks, $p < 0.001$; Fig. 2A). The trend in the mean penile girth was similar to those in the penile girths measured at the distal, mid, and proximal shafts (Fig. 2B–2D).

The mean VAS score for satisfaction with penile appearance increased to a maximum at 4 weeks (1.3±0.1

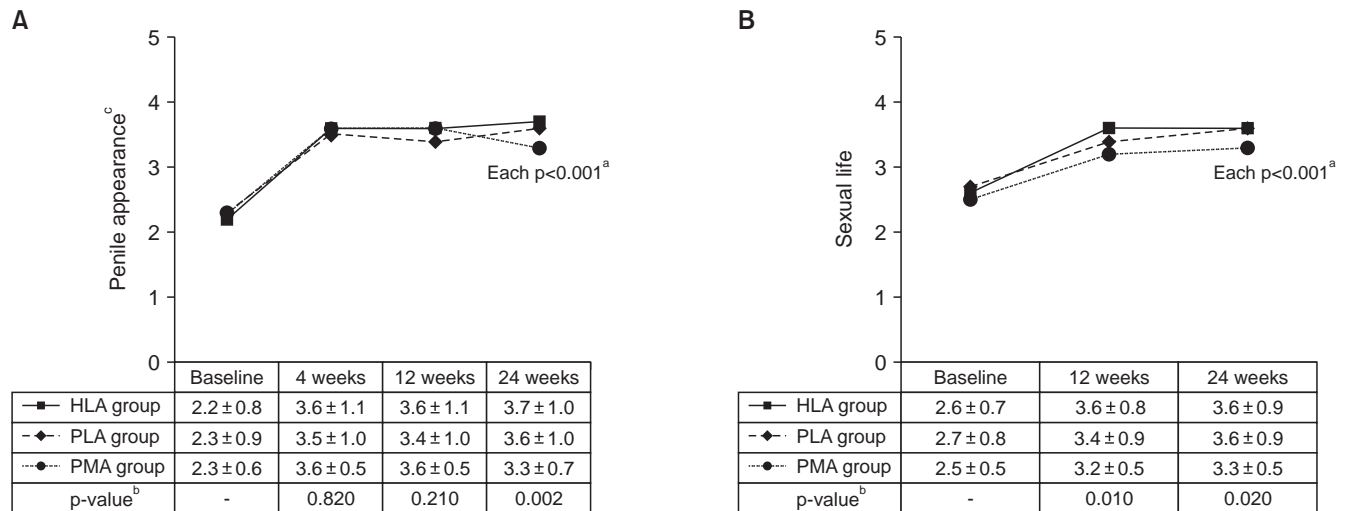


Fig. 3. Changes of satisfaction associated with injections of fillers: (A) penile appearance, (B) sexual life. HLA: hyaluronic acid, PLA: poly lactic acid, PMA: polymethyl methacrylate. ^aPaired t-test. ^bBaseline satisfaction level, baseline penile girth, and change of girth before and after injection-adjusted analysis of covariance test from baseline. ^cSatisfactions were assessed with a 5-point visual analog scale, with 1 indicating very dissatisfied and 5 indicating very satisfied.

score increase, $p < 0.001$) and lasted till 24 weeks (0.1 ± 0.1 score change from 4 to 24 weeks, $p = 0.162$; Fig. 3A). The mean VAS score for satisfaction with sexual life increased till 24 weeks (0.7 ± 0.1 score increase from baseline to 12 weeks, $p < 0.001$; 0.2 ± 0.1 score increase from 12 to 24 weeks, $p = 0.001$; Fig. 3B).

4. PMA filler

At 24 weeks, an increase in penile girth was confirmed with the naked eye (Fig. 1). The penis appeared natural, without nodules or deformities, and the filler material was hard and malleable.

The mean penile girth increased to a maximum at 4 weeks (2.9 ± 0.2 cm increase, $p < 0.001$) and lasted till 24 weeks (0.1 ± 0.1 cm change from 4–24 weeks, $p = 0.440$; Fig. 2A). The trend in the mean penile girth was similar to those in the penile girths measured at the distal, mid, and proximal shafts (Fig. 2B–2D).

The mean VAS score for satisfaction with penile appearance increased to a maximum at 4 weeks (1.3 ± 0.1 score increase, $p < 0.001$), lasted till 12 weeks (0.0 ± 0.0 score change from 12–24 weeks, $p = 0.570$), and then decreased at 24 weeks (0.3 ± 0.1 score decrease from 12–24 weeks, $p = 0.003$; Fig. 3A). The mean VAS score for satisfaction with sexual life increased to a maximum at 12 weeks (0.7 ± 0.1 score increase, $p < 0.001$) and lasted till 24 weeks (0.0 ± 0.1 score change from 12–24 weeks, $p = 0.767$; Fig. 3B).

5. Comparison between fillers

The filler materials were softer and more pliable in the order of HLA, PLA, and PMA, although the penile appearance appeared natural for all filler injections (Fig. 1).

After adjusting for injected filler volume and baseline penile girth, the augmentative effect was greater in the order of PMA, HLA, and PLA, respectively, at 24 weeks (PMA *vs.* HLA, $p < 0.001$; PMA *vs.* PLA, $p < 0.001$; HLA *vs.* PLA, $p = 0.006$; Fig. 2A).

After adjusting for baseline satisfaction level, baseline penile girth, and change in girth after injection, the increase in satisfaction with penile appearance was smaller in the PMA group *versus* the other groups at 24 weeks (PMA *vs.* HLA, $p < 0.001$; PMA *vs.* PLA, $p = 0.007$; and HLA *vs.* PLA, $p = 0.924$). Similarly, the increase in satisfaction with sex life was smaller in the PMA group *versus* the other groups at 24 weeks (PMA *vs.* HLA, $p = 0.007$; PMA *vs.* PLA, $p = 0.054$; HLA *vs.* PLA, $p = 0.704$).

6. Adverse events

In 237 patients (78.7%), penile bruising or swelling was observed 1 day postinjection but spontaneously improved within a week. No significant differences were observed among the groups ($p = 0.748$).

No serious or systemic AEs were observed during the 24 weeks. Filler-associated local AEs were reported in 9 (7.2%), 16 (11.9%), and 6 (14.3%) patients in the HLA,

Table 2. Filler injection-associated local adverse events after injection

Adverse event ^b	HLA group (n=125)		PLA group (n=134)		PMA group (n=42)		p-value
	Cases (%)	Recovery	Cases (%)	Recovery	Cases (%)	Recovery	
Injections site pain	2 (1.6)	Yes	4 (3.0)	Yes	1 (2.4)	Yes	-
Injections site inflammation	3 (2.4)	Yes	3 (2.2)	Yes	1 (2.4)	Yes	-
Injections site nodule	1 (0.8)	Yes ^c	5 (3.7)	No	2 (4.8)	No	-
Injections site pruritis	-	-	2 (1.5)	Yes	1 (2.4)	Yes	-
Penile swelling	2 (1.6)	Yes	-	-	-	-	-
Penile deformity	1 (0.8)	No	2 (1.5)	No	1 (2.4)	No	-
Overall	9 (7.2)		16 (11.9)		6 (14.3)		0.299 ^a

HLA: hyaluronic acid, PLA: polylactic acid, PMA: polymethyl methacrylate.

^aPearson's chi-square test. ^bAdverse events after one week were described. ^cNodule was reversed with hyaluronidase injection.

PLA, and PMA groups, respectively (Table 2). The overall incidence of AEs did not significantly differ between the groups (p=0.299). At 24 weeks, injection site nodules or penile deformities were observed in two (1.6%), seven (5.2%), and three (7.2%) patients in the HLA, PLA, and PMA groups, respectively (p=0.107). However, these were mild, and almost all patients did not want further treatment. Only one patient with a nodule in the HLA group received an injection of hyaluronidase.

DISCUSSION

HLA comprises natural ingredients that have direct, passive, and temporary effects. Although HLA is absorbed into the surrounding tissue over time after injection, the same volume can be maintained with less HLA for several months because the molecules bind to more oxidane during decomposition [4]. Its augmentative effect generally lasts for 6 to 12 months, sometimes up to 18 months [13]. In our study, the augmentative effects were maximal at 4 weeks after injection and then gradually decreased over time. At 24 weeks, they decreased by 19.2% compared to the maximum effects. These trends are similar to those reported in previous studies [6-9].

PLA is a biodegradable and reabsorbable synthetic polymer with delayed, biostimulatory, and temporary effects [4]. PLA induces cellular inflammatory responses, stimulating fibroblast proliferation and neocollagenesis [14]. Its liquid component is absorbed over a few days after injection. Over the next 1 to 3 months, the PLA microparticles are gradually absorbed by hydrolysis, whereas subtle volume expansion occurs *via* a fibrous reaction and collagen deposition. Over time, the volume decreases

steadily. Its augmentative effect generally lasts for 18 to 24 months, sometimes up to 36 months [10,15]. In our study, the augmentative effects were maximal at 12 weeks after injection and then gradually decreased over time. At 24 weeks, they decreased by 14.3% compared to the maximum effect. These trends are similar to those reported in previous studies [6-9].

PMA is a non-absorbable synthetic polymer with a permanent effect [4]. After injection, the PMA microspheres were encapsulated in endogenously derived connective tissue composed of macrophages, fibroblasts, and collagen [16]. Encapsulation prevents microsphere migration and phagocytosis. Additionally, PMA is not degraded by enzymatic digestion. In our study, its augmentative effects were maximal 4 weeks after injection and lasted for up to 24 weeks. These trends are similar to those reported in previous studies [11,17].

To date, an ideal filler for PAs has not been developed, although several types of fillers have been introduced. Therefore, it is important to understand the differences in the clinical characteristics of the available fillers. Nevertheless, to our knowledge, no studies have compared the efficacy and safety of the three fillers (HLA, PLA, and PMA) most commonly used for PA [15,18,19]. Our study was the first to compare the clinical outcomes of HLA, PLA, and PMA filler injections. At 4 weeks, the augmentative effects of HLA and PMA filler injections were comparable but larger than those of PLA filler injections (data not shown). However, from week 12 onwards, the augmentative effect increased in the order of PMA, HLA, and PLA filler injections. Consistent with our results, a recent meta-analysis showed that the augmentative effects of HLA fillers were greater than those of PLA fillers [20].

In evaluating the clinical utility of PA, patient satis-

faction is as important as the penile augmentative effect because PA is almost always performed according to the patient's needs. In our study, satisfaction levels increased after filler injections and were adequately maintained in all filler groups, even when the augmentative effects gradually decreased. These results indicate that PA-associated satisfaction levels may not be affected solely by the penile appearance or size. Also, penile augmentative effects and satisfaction levels were not proportional. These results suggest that an increase in penile size may not have a direct effect on PA-associated satisfaction but may be a trigger.

Contrary to the results comparing the augmentative effects between the fillers, the increases in satisfaction levels were smaller in the PMA group than in the other groups at 24 weeks. It is unclear why these results were derived, but some explanations may be suggested. First, the PMA was harder than the HLA and PLA, making the penis feel more unnatural. Second, the PMA have a permanent augmentative effect, while the HLA and PLA have only a temporary augmentative effect [4,12]. This nature of PMA may cause anxiety and decrease of satisfaction levels in patients, because it is difficult to reverse the results of PA. Finally, although there were statistically significant differences in satisfaction levels between the fillers, further researches are needed to clarify whether these differences are clinically significant.

Penile infection, erythema, bruising, swelling, nodules, and deformities are common AEs that occur after filler injections and are mild and transient in most cases [4,15]. Serious AEs, such as tissue necrosis and filler migration, are rare. Previous studies have reported local AEs in 3% to 9% of patients for HLA [6-9], 6% to 24% for PLA [6-10], and 1% to 11% for PMA [11,17]. These are consistent with findings from our study. There was no significant difference in the overall incidence of local AEs among the groups. The safety of the three fillers in our study was comparable and superior to that of invasive surgeries [18,19,21].

Our study has some limitations. First, our study was conducted at a single center. Therefore, our results may not be directly applied to clinical practice, because they cannot be generalized. Second, the follow-up duration after filler injection was insufficient to prove the long-term efficacy and safety. Particularly, HLA and PLA fillers have only a temporary augmentative effect; therefore, long-term observation is important to confirm

their clinical utility. Third, the type of filler was decided in consultation with the patients; therefore, the efficacy of the filler may have been exaggerated. However, PA is performed according to the patient's subjective needs and not the pathological disease. Therefore, our results may better reflect the clinical utility of fillers than those of randomized controlled trials in actual clinical settings. Finally, the erect state of the penis was not assessed. Previous studies suggest that a flaccid, rather than erect, penile girth is more likely to cause distress in men complaining of a small penis [22-24]. Nevertheless, assessment of erect penile girths may provide more comprehensive information regarding PA.

CONCLUSIONS

Our study demonstrated that all three fillers (HLA, PLA, and PMA) for PA led to significant increases in penile girth and injection-associated satisfaction levels without serious AEs. However, the augmentative effect at 24 weeks was larger in the order of PMA, HLA, and PLA, respectively, whereas the increase in satisfaction levels was smaller for the PMA filler than for the other two fillers. Furthermore, the postinjection clinical changes in penile girth and satisfaction levels over time differed significantly between the fillers.

Our study demonstrated the clinical course of different types of fillers and suggested that the filler type should be selected after detailed counseling considering individual characteristics and preferences.

Conflict of Interest

The authors have nothing to disclose.

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Author Contribution

Conceptualization: DYY, WKL. Data curation: DWK, WKL. Formal analysis: DWK, THK, WKL. Investigation: DWK, WKL. Methodology: HCJ, KK, DYY, JKK, SHL, THK, WKL. Project

administration: WKL. Resources: DYY, SHL, WKL. Software: WKL. Supervision: DYY, SHL, WKL. Writing – original draft: DWK. Writing – review & editing: WKL.

Data Sharing Statement

The data required to reproduce these findings cannot be shared at this time as the data also forms part of an ongoing study.

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