



Efficacy and complications of hyaluronic acid and poly lactic acid for penile augmentation: a systematic review and meta-analysis

Ahmad Kusumaputra, MD, Muhammad R. Setiawan, MD, Mohammad A. Soebadi, PhD, Soetojo Wirjopranoto*

Background: Penile size is considered a symbol of manhood and is a subjective problem for men, especially those with small penis syndrome. Penile augmentation was introduced to correct penile size problems from a medical, psychological, or esthetic point of view. Hyaluronic acid (HA) and poly lactic acid (PLA) are two types of augmentation agents that are popularly used today. However, no systematic studies and meta-analyses have compared these two modalities as penile augmentation agents. This study aimed to analyze the efficacy and safety of penile filler injections with HA compared to PLA.

Methods: This study was based on the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines. Articles examining the differences in efficacy and adverse events of the administration of HA and PLA in patients undergoing penile augmentation were systematically reviewed from the PubMed, Proquest, Web of Science, and Scopus databases. An odds ratio with a 95% CI was applied to measure the study outcome. The analysis was performed with RevMan 5.4 software. The risk of bias for each study was evaluated using the Risk of Bias v2 instrument from Cochrane. This research protocol is registered in the International Prospective Register of Systematic Reviews (PROSPERO) registry.

Result: Four articles consisting of 283 research subjects were included in this study. The meta-analysis for penile girth enhancement after penile augmentation found significant results in the HA group compared to the PLA group ($P = 0.01$). There was no difference in the level of satisfaction with penile appearance 4 weeks after penile augmentation in the HA group compared to the PLA group ($P = 0.79$). HA was significantly superior in sexual satisfaction 12 weeks postpenile augmentation ($P = 0.0004$). There was no difference in the incidence of pain after penile augmentation in the HA group compared to the PLA group ($P = 0.33$). In the postaugmentation penile inflammation, there was no difference ($P = 0.98$) in the HA group compared to the PLA group.

Conclusion: There are differences in the efficacy of penile augmentation with the superiority of HA in increasing penile diameter and postaugmentation sexual satisfaction compared to PLA. There was no difference in the incidence of complications between using HA and PLA.

Keyword: hyaluronic acid, poly lactic acid, penile augmentation, penile filler

Introduction

Penile girth enhancement (PGE) has been introduced in the treatment of patients with sexual dysfunction and anatomic abnormalities such as penile curvature^[1,2]. Medical and psychological issues can be addressed with several penile augmentation methods. Small penis syndrome (SPS) is excessive anxiety about a penis that is smaller than normal for adult men, despite a

Department of Urology, Faculty of Medicine, Universitas Airlangga, Surabaya, East Java, Indonesia

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Jl. Mayjen Prof Dr Moestopo No. 47, Pacar Kembang, Tambaksari, Kota Surabaya, Jawa Timur 60132, Indonesia. Tel.: +62 31 5017404, fax: +62 31 5024971. E-mail: s.tojowirjopranoto@yahoo.com (S. Wirjopranoto).

Copyright © 2023 The Author(s). Published by Wolters Kluwer Health, Inc. 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.

Annals of Medicine & Surgery (2023) 85:4531–4538

Received 6 May 2023; Accepted 13 July 2023

Published online 22 July 2023

<http://dx.doi.org/10.1097/MS9.0000000000001094>

HIGHLIGHTS

- This systematic review and meta-analysis compared the efficacy and safety of hyaluronic acid and poly lactic acid for penile enlargement.
- The results showed that hyaluronic acid increased penile diameter more and had better patient satisfaction than poly lactic acid.
- The meta-analysis also found that hyaluronic acid and poly lactic acid semi-permanent penile augmentation is safe and effective. Still, more research is needed to determine its long-term physical and psychological effects before it can be recommended.
- We concluded that hyaluronic acid is superior to poly lactic acid because it offers more benefits to the patient.

normal clinical examination^[3]. If initial SPS interventions fail, penile augmentation may be considered^[3,4].

Hyaluronic acid was FDA-approved as a filler in 2003. Since 2004, hyaluronic acid penile enlargement for premature ejaculation has gained popularity, especially in Asia^[1]. Hyaluronic acid is biocompatible and lasts longer than other fillers. Hyaluronic acid has been shown to enlarge peniles in recent studies^[5,6]. Common fillers include poly lactic acid. Poly lactic acid biostimulates fibroblast proliferation and neo-collagenesis, unlike hyaluronic acid.

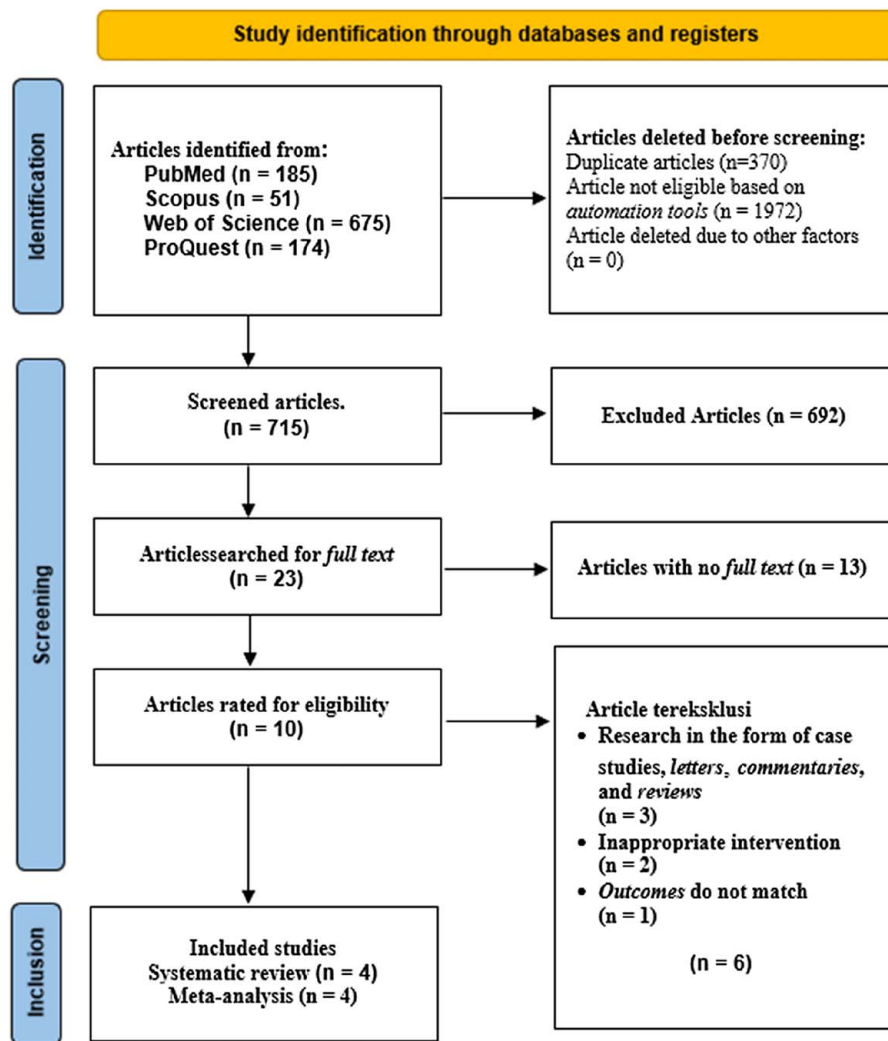


Figure 1. Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) flow diagram.

Poly lactic acid induces dermal fibroplasia and foreign body inflammation to augment tissue^[7]. Hyaluronic acid and poly lactic acid enhance penile girth for 18 months without side effects^[6,8].

While surgical PGE procedures are still limited, demand is rising^[9]. Cosmetic goals require safe, effective, and minimally invasive methods. PGE is based on the patient's needs, so it is important to compare the clinical outcomes of different fillers. Cosmetic goals require safe, effective, and minimally invasive methods. PGE is based on the patient's needs, so it is important to compare clinical outcomes of different fillers. This systematic review and meta-analysis compared the efficacy and safety of hyaluronic acid and poly lactic acid for penile enlargement. We found no PROSPERO-registered studies or meta-analyses on PGE with hyaluronic acid or poly lactic acid, so we designed this study to compare their efficacy and side effects.

Methods

Study design

This review followed the Cochrane Handbook for Systematic Reviews of Interventions and the Preferred Reporting Items for

Systematic Review and Meta-Analysis (PRISMA)^[10]. The protocol of this review has been registered in the International Prospective Register of Systematic Reviews (PROSPERO), maintained by the National Institute for Health Research (NIHR), and contains information about this study (Identification number CRD42023188174). Since the information was accessible to the general public, institutional review board (IRB) approval was not necessary. We also self-evaluate the quality of our systematic review using AMSTAR 2 criteria^[11].

Systematic search strategy

A systematic search using medical subject heading (MeSH) terms with the Boolean operator was performed in PubMed, Scopus, ScienceDirect, and ProQuest databases for studies published up to March 2023. The primary keywords used in the searching process were as follows: *small penis syndrome, penile augmentation, penile enhancement, hyaluronic acid, poly lactic acid, HA, and PLA*.

Data extraction

Three independent examiners collected article information, including authors, publication date, study location, and sample

Table 1**Baseline characteristics of the research population**

References	Country	Design	Follow-up (weeks)	Age	n	Group	Types of fillers (trade name)	Mean vol. injection, ml (mean ± SD)	Injection materials	Outcomes
Yang <i>et al.</i> ^[5] 2019a	Korea	RCT	48	20–65	36	Intervention	Hyaluronic acid (Chaeum Shape)	19.14 ± 1.4	20 mg/ml HA cross-linked	Penile girth, satisfaction rate appearance, sexual satisfaction level, side effects
					34	Control	Polylactic acid (PowerFill)	20.59 ± 1.28	10 g/3 ml microparticles PLA	
Yang <i>et al.</i> ^[22] 2019b	Korea	RCT	24	19–65	37	Intervention	Hyaluronic acid (Neuramis Deep)	20.8 ± 1.5	20 mg/ml HA cross-linked	Penile girth, satisfaction rate appearance, sexual satisfaction level, side effects
					35	Control	Polylactic acid (PowerFill)	21.8 ± 1.7	10 g/3 ml microparticles PLA	
Yang <i>et al.</i> ^[6] 2020	Korea	RCT	72	20–66	33	Intervention	Hyaluronic acid (Hyafilia Impact)	16.4 ± 2.7	20 mg HA cross-linked + 3 mg lidocaine/ml	Penile girth, satisfaction rate appearance, sexual satisfaction level, side effects
					34	Control	Polylactic acid (PowerFill)	17.7 ± 2.3	10 g/3 ml microparticles PLA	
Ahn <i>et al.</i> ^[17]	Korea	RCT	24	20–65	32	Intervention	Hyaluronic acid (Doublofill)	15–22	23 mg HA cross-linked + 3 mg lidocaine/2 ml	Penile girth, sexual satisfaction rate, side effects
					32	Control	Polylactic acid (PowerFill)	15–22	10 g/3 ml microparticles PLA	

PLA, polylactic acid.

Table 2**Outcome profile inclusion study systematic review and meta-analysis**

References	Types of fillers (trade name)	Increase in penile diameter, mm (mean ± SD)	Improved penile appearance satisfaction, VAS score* (mean ± SD)	Increased sexual satisfaction, VAS score* (mean ± SD)	Pain events (n)	Penile inflammatory events (n)
Yang <i>et al.</i> ^[5] 2019a	Hyaluronic acid (Chaeum Shape)	20.6 ± 10.9	1.59 ± 1.13	1.13 ± 1.24	0	0
	Polylactic acid (PowerFill)	14.6 ± 10.4	1.5 ± 1.26	0.88 ± 1.56	1	1
Yang <i>et al.</i> ^[22] 2019b	Hyaluronic acid (Neuramis Deep)	21 ± 10	1.7 ± 1.7	1.1 ± 1	0	1
	Polylactic acid (PowerFill)	16 ± 9	1.7 ± 1.4	0.4 ± 1.1	2	0
Yang <i>et al.</i> ^[6] 2020	Hyaluronic acid (Hyafilia Impact)	19.1 ± 14.9	1.2 ± 1.1	1.1 ± 0.9	2	1
	Polylactic acid (PowerFill)	19.5 ± 10.8	1.4 ± 1	0.9 ± 1.2	1	1
Ahn <i>et al.</i> ^[17]	Hyaluronic acid (Doublofill)	22.7 ± 12.6	TD	1.16 ± 1.07	0	2
	Polylactic acid (PowerFill)	20.2 ± 8.73	TD	0.42 ± 0.89	1	2

*VAS Score: Visual Analogue Scale Score

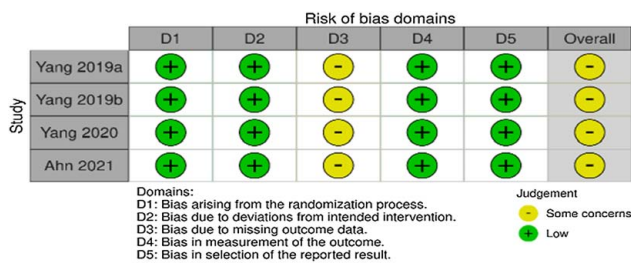


Figure 2. Evaluation of the risk of bias with the Cochrane risk of bias tool v2.

size. Along with penile augmentation, baseline characteristics like mean age, filler type, average volume of injection, injection material, outcome, and evaluation were extracted. These include PGE, VAS-improved penile appearance, sexual satisfaction, pain events, and penile inflammation. If data extraction disagrees, the third examiner will be consulted.

Statistical analysis

Postoperative follow-up revealed study endpoints. The SMD and 95% CI were used to calculate the SD from the mean for continuous variables. The odds ratio (OR) was used to estimate the outcome of the interest difference between groups. Heterogeneity analysis is generated as the index of I^2 , of which the value > 50% along with $P < 0.05$ was judged to be significant. Thus, a random-effects model will analyze the pooled outcome. Fixed-effects analysis is justified by low heterogeneity. This systematic review and meta-analysis uses Revman 5.4.1 by the Cochrane Collaboration for statistics.

Assessment of study quality

Cochrane risk of bias (RoB) 2.0 will evaluate randomized controlled trials (RCTs) for the randomization process, deviations from the intended intervention, missing outcome data, measurement of the outcome, and selection of the reported result.

Results

Systematic search result

The PRISMA flow diagram (Fig. 1) shows article searching and selection. Four online databases yielded 1085 initial articles for the systematic study. Table 1 shows search engine results. Three hundred and seventy duplicate articles were removed from the

acquisition during screening. Twenty-three studies were extractable and candidates for eligibility evaluation after the primary screening, resulting in ten studies that were thoroughly evaluated according to study criteria. Qualitative synthesis and meta-analysis included four studies. The flowchart shows the PRISMA-guided systematic literature search.

Characteristics of the pooled studies

All four inclusion studies were RCTs with 283 participants. Tables 1 and 2 present baseline characteristics and extracted study data. Four (2019–2021) studies had 24– 72-week follow-ups. Each study included 19–66-year-olds. Two clinical trial protocol groups exist. A different product with 20 mg/ml cross-linked hyaluronic acid filler is used. One study found 23 mg cross-linked HA and 3 mg lidocaine/2 ml. The four studies used the 10 g/3 ml PLA microparticle injection material’s poly lactic acid filler. The two intervention groups had 16.4–20.8 ml injection volumes. Each study examined penile girth, satisfaction with penile appearance, sexual satisfaction, and postenlargement side effects like penile pain and swelling.

Assessment of study quality and risk of study bias

This systematic review and meta-analysis included RCT clinical trials, so the Cochrane RoB v2 instrument could assess research bias. Five domains were assessed sequentially: participant selection bias (randomization), deviation from intervention protocols, unreported or incomplete study data, means of measuring outcomes, and likelihood of selectively reported outcomes. The final score was determined according to the algorithm described by Higgins *et al.*^[12], showed that the three RCTs conducted by Yang *et al.* and research by Ahn *et al.* RoB toward the third domain. Protocol deviations, personal choices, withdrawal of consent, and loss of follow-up caused withdrawals in every study. Figure 2 summarizes assessment results.

Meta-analysis of PGE postaugmentation with HA versus PLA fillers

The forest plot compares the mean penile girth increase in the two study groups. HA increased penile diameter more than PLA in four studies with 262 participants (SMD 0.31; 95% CI: 0.07–0.65; $P = 0.01$). Due to low study heterogeneity, the forest plot (Fig. 3) used the fixed-effects model ($I^2 = 18\%$).

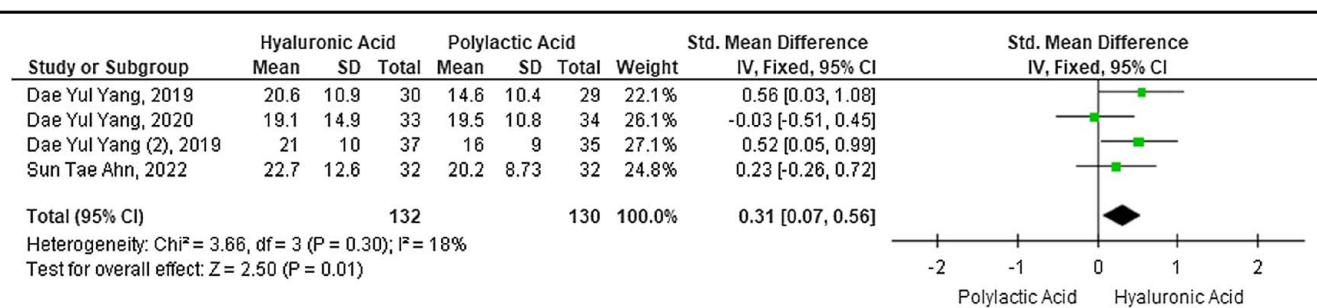


Figure 3. Forest plot of penile girth enhancement after penile augmentation with hyaluronic acid versus poly lactic acid fillers.

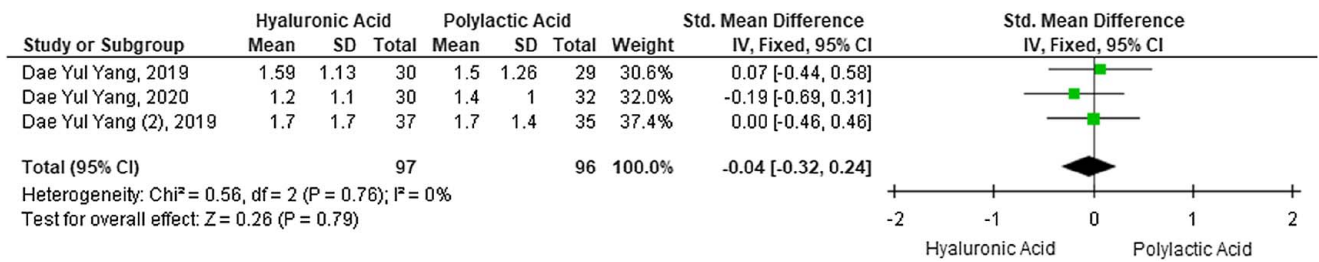


Figure 4. Forest plot of satisfaction with penile appearance 4 weeks after penile augmentation with hyaluronic acid versus polylactic acid fillers.

Meta-analysis of satisfaction with penile appearance 4 weeks after penile augmentation with HA versus PLA fillers

Contrary to penile enlargement results, a meta-analysis on a subjective scale of satisfaction with penile appearance 4 weeks after penile augmentation showed no difference between the HA and PLA intervention groups (SMD -0.04; 95% CI: -0.32 to 0.24; P = 0.79) involving three studies and 193 participants (Fig. 4). These outcomes were analyzed using the fixed-effects model due to low heterogeneity between studies with an I² of 0%.

Meta-analysis of levels of sexual satisfaction 12 weeks postpenile augmentation with HA versus PLA fillers

The next major outcome was the difference in sexual satisfaction between the two study groups 12 weeks after the augmentation. A meta-analysis of four studies with 257 participants found a significant difference in sexual satisfaction between the two intervention groups (SMD 0.45; 95% CI: 0.20-0.70; P = 0.0004), HA filler outperforms PLA. Forest plots (Fig. 5) used the fixed-effects model due to low study heterogeneity (I² = 29%).

Meta-analysis of postaugmentation pain incidence with HA fillers versus PLA

The OR from each study’s dichotomous data was used to estimate pain side effects. HA injection did not increase pain compared to PLA (OR 0.52) (95% CI: 0.14-1.94; P = 0.33). Analysis of heterogeneity between studies resulted in an index of I² = 0%, so study heterogeneity was not significant. The forest plot shown in Figure 6 uses the fixed effect model based on the heterogeneity test results of the four studies.

Meta-analysis of postaugmentation inflammatory incidence with HA versus PLA fillers

The incidence of postaugmentation penile inflammation was analyzed as an OR using dichotomous data. The results of the meta-analysis showed no difference in the incidence of penile inflammation as indicated by an OR of 0.98 (95% CI: 2.80-3.50; P = 0.98). Analysis of heterogeneity between studies resulted in an index of I² = 0%, so it can be said that heterogeneity between studies was not significant. A meta-analysis was carried out using the fixed effect model based on the heterogeneity test results. A collection of meta-analyses of the adverse effects of penile inflammation are shown in the forest plots in Figure 7.

Discussions

For years, men have sought penile enlargement surgeries for medical and nonmedical reasons^[13]. SPS patients, who may have unrealistic penile size and appearance expectations, must be treated carefully^[13]. Hyaluronic acid and polylactic acid fillers are now preferred for penile augmentation over autologous fat, silicone, and polymethylmethacrylate due to biomaterials advancements that improve results and reduce patient downtime^[13,14]. Several isolated and comparative studies have shown both fillers to be safe and effective^[6,8,15,16].

Four RCT clinical trials from South Korea met this study’s methodological and outcome requirements, according to a comprehensive literature search. These studies have 24 to 72-week follow-ups. Hyaluronic acid and polylactic acid metabolism stabilizes 24 weeks after injection^[13,17]. Due to the rapid development of esthetic surgery and the higher proportion of men who undergo esthetic surgery in South Korea, more studies on penile augmentation are likely to be discovered there^[18]. Four inclusion studies used monophasic and biphasic HA products with

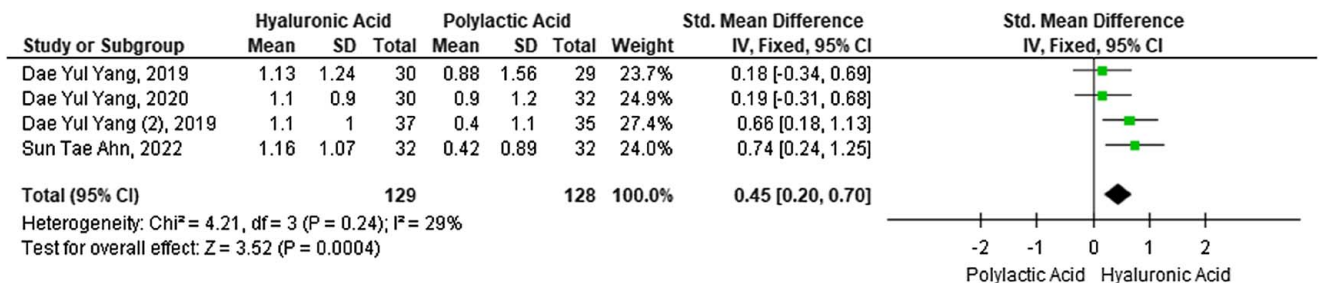


Figure 5. Forest plot of sexual satisfaction level 12 weeks after penile augmentation with hyaluronic acid versus polylactic acid filler.

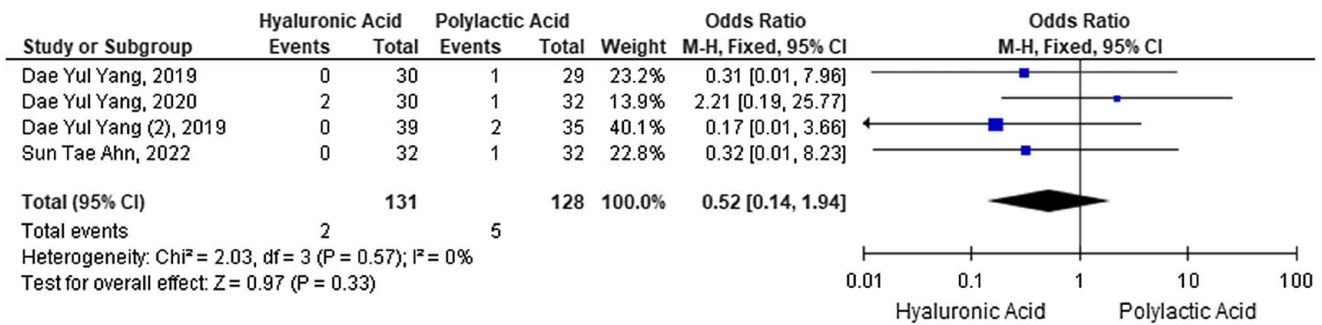


Figure 6. Forest plot of the incidence of post-augmentation pain with hyaluronic acid versus polylactic acid fillers.

comparable doses but different cross-linking structures. High-cross-linked HA increases filler viscosity and cohesiveness, resulting in a longer-lasting augmentative effect. This decreases HA biocompatibility, increasing the risk of adverse effects like local responses, discomfort, edema, and granulomas^[9,19]. After biphasic and monophasic HA injection, the dermis has a large pool of HA in the lower dermis and no HA in the upper and middle reticulate dermis, according to histological studies. Monophasic products better distribute HA particles across the dermis, but in large clusters^[20].

The pooled meta-analysis showed that hyaluronic acid increased penis diameter more than polylactic acid for penile girth enlargement. In a recent prospective study by Zhang *et al.*^[21], which used HA gel injection with similar material and average injection volume (21.5 ± 3.7 ml) and followed patients for 1-year postinjection, penis diameter, and length increased significantly in both flaccid and erectile phases. One of the four RCTs in this meta-analysis showed comparable clinical efficacy between HA and PLA with an average maximum addition size of 2.5 cm and 2.3 cm, respectively^[6]. HA is naturally absorbed into the bloodstream faster than PLA, which is synthetic^[14]. The uniformly distributed HA gel's hydrophilic strength increases volume and weight, preventing the penis corpus from contracting, especially when flaccid^[21].

Penile appearance satisfaction both fillers were similar 4 weeks post-augmentation. The four inclusion studies show that HA and PLA fillers are significantly more satisfying than baseline without penile augmentation. Filler increases the penile diameter. HA and PLA fillers improve penile esthetics after augmentation^[5,6,22,23].

After segmentation, the hyaluronic acid filler group had greater sexual pleasure. A review of nonsurgical penile augmentation

techniques found that HA increases satisfaction^[24]. In the study by Ahn *et al.*, some patients had a reduction in ejaculation-related symptoms, which is intriguing. Several research have demonstrated the efficiency of penile glans augmentation using HA fillers; nevertheless, the effects of ejaculation on penile augmentation with HA fillers remain unknown. Hyaluronic acid-based penile fillers infiltrate the buck and dartos fascias. Hyaluronic acid fillers can increase the threshold of penile dorsalis nervus receptors by blocking tactile stimuli. Obviously, this can boost patient's pleasure with their sexual performance if they have HA fillers^[23]. SPS patients have normal libidos, and therapies reduce their psychological suffering^[25,26]. Two studies added lidocaine to HA fillers. Smith *et al.* found that lidocaine-containing HA fillers significantly reduced pain during and after injection without changing side effects. Safe and comfortable penile augmentation may improve patient satisfaction^[27].

Hyaluronic acid and polylactic acid fillers cause similar post-augmentation penile discomfort and inflammation. HA had 1.5% penile discomfort and inflammation, while PLA had 3.9 and 3%. Another study found penile injection with HA or PLA was statistically safe and most side effects resolved spontaneously^[28]. Zhang *et al.* found two cases of penile edema and one case of subcutaneous hemorrhage after HA and PLA penile injections with a 1-year follow-up. Both cases improved spontaneously within 4 weeks^[21].

The study shows that hyaluronic acid and polylactic acid semi-permanent penile augmentation is safe and effective. The researcher's view is consistent with previous systematic studies that found penile augmentation can be an option for patients, but clinically this modality is controversial, so more research is

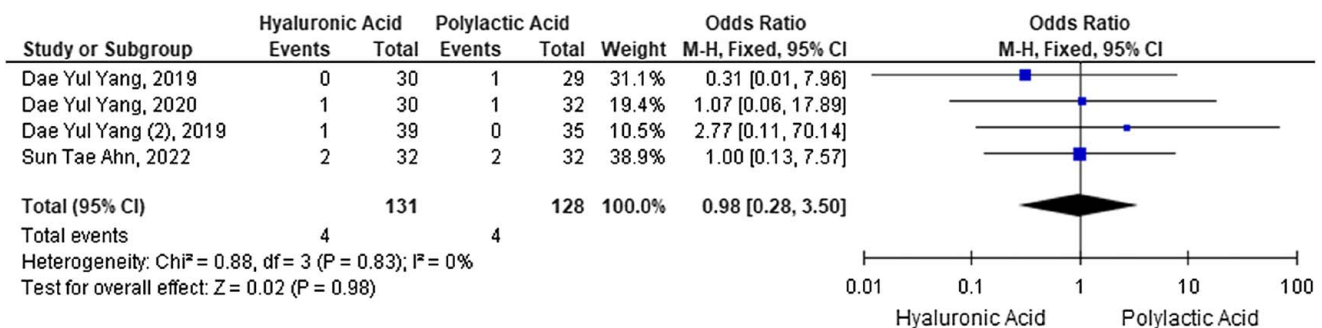


Figure 7. Forest plot of inflammatory incidence after penile augmentation with hyaluronic acid versus polylactic acid fillers.

Table 3**Case reports of postaugmentation complications of the penile**

References	Country	Age (years)	Filler material	Onset	Complications
Khor <i>et al.</i> ^[31]	Australia	31	Hyaluronic acid	2 bulan	Fulminan penile infection
Al-maghlouth <i>et al.</i> ^[29]	Saudi Arabia	41	Hyaluronic acid	4 tahun	Penile abscess
Bryce <i>et al.</i> ^[30]	USA	56	Hyaluronic acid	2 minggu	Dermatitis

needed to determine its long-term physical and psychological effects before it can be recommended^[14,24].

HA fillers can cause severe infections, including fatal sepsis, after penile augmentation, as shown in Table 3. Abscesses and sepsis can result from filler biofilms^[29–31]. Biofilms protect bacteria from antibiotic bactericides but harm cultures. Immunosuppression, trauma, or iatrogenic manipulation can activate latent biofilm microorganisms. Postaugmentation sexual activity spreads bacteria from the penile, pubic hair, and vagina. Sexual activity should wait at least 1 month after augmentation to heal the filler injection wound^[28,31,32]. Rare side effects may be late-onset due to the limited number of documented cases and short follow-up period. Superfluous preputium in uncircumcised patients can alter negative effects. Standard injection protocols and aseptic preoperative preparations reduce complications^[28].

This study's limitations include the small sample size of fewer than 10 studies, which precludes publication bias analysis. There are differences in cross-linking methods and monophasic/biphasic types of hyaluronic acid preparations used, although the injection dose and volume are comparable. The length of follow-up in inclusion studies is still variable and may not be sufficient to describe the true durability of the outcome. Because there is no group division based on dose titration, the optimal recommended dose of injectable filler is inconclusive. Currently, there is no standardized method for measuring postaugmentation satisfaction. In the study of inclusion, it was also discovered that three of the four studies had the same first author, allowing for bias. In addition, this systematic review and meta-analysis require additional studies involving multicenter participants from different countries and researchers in order to enhance external validation.

Conclusion

Our systematic review and meta-analysis found that HA filler improves penile girth and sexual satisfaction 12 weeks after penile augmentation compared to PA. HA filler improved penile girth and sexual satisfaction in this study.

Ethical approval

Ethical approval is not required in this type of study.

Consent

Informed consent is not required in this type of study.

Sources of funding

The authors received no financial support for this work.

Author contribution

A.K., M.R.S., and J.R.: concept; A.K., M.R.S., M.A.S., and S.W.: design; M.A.S. and S.W.: supervision; A.K., M.R.S., M.A.S., and S.W.: resources; A.K., M.R.S., M.A.S., and S.W.: materials; A.K., M.R.S., M.A.S., and S.W.: data collection and/or processing; A.K., M.R.S., M.A.S., and S.W.: analysis and/or interpretation; A.K., M.R.S., M.A.S., and S.W.: literature search; A.K., M.R.S., M.A.S., and S.W.: writing manuscript; A.K., M.R.S., M.A.S., and S.W.: critical review.

Conflicts of interest disclosure

The authors declare that there is no competing interest.

Research registration unique identifying number (UIN)

1. Name of the registry: not applicable.
2. Unique identifying number or registration ID: not applicable.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): not applicable.

Guarantor

Prof Soetojo Wirjopranoto.

Data availability statement

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

Provenance and peer review

Not commissioned, externally peer-reviewed.

Acknowledgements

None.

References

- [1] Abdallah H, Abdelnasser T, Hosny H, *et al.* Treatment of premature ejaculation by glans penis augmentation using hyaluronic acid gel: a pilot study. *Andrologia* 2011;44:650–3.
- [2] Chung E. Penile reconstructive surgery in peyronie disease: challenges in restoring normal penis size, shape, and function. *World J Mens Health* 2020;38:1–8.
- [3] Wylie KR, Eardley I. Penile size and the 'small penis syndrome'. *BJU Int* 2007;99:1449–55.

- [4] Ghanem H, Glina S, Assalian P, *et al.* Position paper: management of men complaining of a small penis despite an actually normal size. *J Sex Med* 2013;10:294–303.
- [5] Yang DY, Ko K, Lee SH, *et al.* A comparison of the efficacy and safety between hyaluronic acid and poly(lactic acid) filler injection in penile augmentation: a multicenter, patient/evaluator-blinded, randomized trial. *J Sex Med* 2019;16:577–85.
- [6] Yang DY, Jeong HC, Ko K, *et al.* Comparison of clinical outcomes between hyaluronic and poly(lactic acid) filler injections for penile augmentation in men reporting a small penis: a multicenter, patient-blinded/evaluator-blinded, non-inferiority, randomized comparative trial with 18 months of follow-up. *J Clin Med* 2020;9:1024.
- [7] Hyun MY, Lee Y, No YA, *et al.* Efficacy and safety of injection with poly-L-lactic acid compared with hyaluronic acid for correction of nasolabial fold: a randomized, evaluator-blinded, comparative study. *Clin Exp Dermatol* 2014;40:129–35.
- [8] Kwak T, Oh M, Kim J, *et al.* The effects of penile girth enhancement using injectable hyaluronic acid gel, a filler. *J Sex Med* 2010;8:3407–13.
- [9] Goldberg DJ. Breakthroughs in US dermal fillers for facial soft-tissue augmentation. *J Cosmet Laser Ther* 2009;11:240–7.
- [10] Page MJ, McKenzie JE, Bossuyt PM, *et al.* The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Int J Surg* 2021;88:105906.
- [11] Shea BJ, Reeves BC, Wells G, *et al.* AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ (Online)* 2017;358:j4008.
- [12] Higgins JPT, Altman DG, Gøtzsche PC, *et al.* The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928.
- [13] Park NC, Kim SW, Moon DG. *Penile Augmentation*. Springer; 2016.
- [14] Xing MH, Hou SW, Raheem OA. Aesthetic penile augmentation procedures: a comprehensive and current perspective. *Curr Urol Rep* 2022;23:355–61.
- [15] Yang DY, Ko K, Lee SH, *et al.* Efficacy and safety of a newly developed poly(lactic acid) microsphere as an injectable bulking agent for penile augmentation: 18-months follow-up. *Int J Impot Res* 2017;29:136–41.
- [16] Yang DY, Ko K, Lee SH, *et al.* Efficacy and safety of newly developed cross-linked dextran gel injection for glans penis augmentation with a novel technique. *Asian J Androl* 2018;20:80–4.
- [17] Ahn ST, Shim JS, Bae WJ, *et al.* Efficacy and safety of penile girth enhancement using hyaluronic acid filler and the clinical impact on ejaculation: a multi-center, patient/evaluator-blinded, randomized active-controlled trial. *World J Mens Health* 2021;39:299.
- [18] Holliday R, Elfving-Hwang J. Gender, globalization and aesthetic surgery in South Korea. *Body Soc* 2012;18:58–81.
- [19] Herrmann JL, Hoffmann RK, Ward CE, *et al.* Biochemistry, physiology, and tissue interactions of contemporary biodegradable injectable dermal fillers. *Dermatol Surg* 2018;44:S19–31.
- [20] Flynn TC, Sarazin D, Bezzola A, *et al.* Comparative histology of intradermal implantation of mono and biphasic hyaluronic acid fillers. *Dermatol Surg* 2011;37:637–43.
- [21] Zhang CL, Quan Y, Li H, *et al.* Penile augmentation with injectable hyaluronic acid gel: an alternative choice for small penis syndrome. *Asian J Androl* 2022;24:601–6.
- [22] Yang DY, Jeong HC, Ahn ST, *et al.* A comparison between hyaluronic acid and poly(lactic acid) filler injections for temporary penile augmentation in patients with small penis syndrome: a multicenter, patient/evaluator-blind, comparative, randomized trial. *J Sex Med* 2019;17:133–41.
- [23] Ahn ST, Shim JS, Bae WJ, *et al.* Efficacy and safety of penile girth enhancement using hyaluronic acid filler and the clinical impact on ejaculation: a multi-center, patient/evaluator-blinded, randomized active-controlled trial. *World J Mens Health* 2022;40:299–307.
- [24] Salloum A, Bazzi N, Haber R. Nonsurgical methods for penile augmentation: a systematic review. *Dermatol Surg* 2021;47:e81–5.
- [25] Veale D, Miles S, Read J, *et al.* Sexual functioning and behavior of men with body dysmorphic disorder concerning penis size compared with men anxious about penis size and with controls: a cohort study. *Sex Med* 2015;3:147–55.
- [26] Yang DY, Jeong HC, Ahn ST, *et al.* A comparison between hyaluronic acid and poly(lactic acid) filler injections for temporary penile augmentation in patients with small penis syndrome: a multicenter, patient/evaluator-blind, comparative, randomized trial. *J Sex Med* 2020;17:133–41.
- [27] Smith L, Cockerham K. Hyaluronic acid dermal fillers: can adjunctive lidocaine improve patient satisfaction without decreasing efficacy or duration. *Patient Prefer Adherence* 2011;5:133–9.
- [28] Quan Y, Gao ZR, Dai X, *et al.* Complications and management of penile augmentation with hyaluronic acid injection. *Asian J Androl* 2021;23:392–5.
- [29] Al-Maghlouth AK, Alwesali S, Faqeeh A, *et al.* Late onset penile abscess after 4 years from hyaluronic acid injection. A rare case report. *Urol Case Rep* 2021;37:101632.
- [30] Baird Bryce A, Robertson N, Broderick Gregory A. Penile girth injection complications: a case report. *Sex Med* 2021;9:100445.
- [31] Khor NWM, Dhar A, Cameron-Strange A. The perils of penile enhancement: case report of a fulminant penile infection. *BMC Urol* 2021;21:115.
- [32] Marusza W, Olszanski R, Sierdzinski J, *et al.* Treatment of late bacterial infections resulting from soft-tissue filler injections. *Infect Drug Resist* 2019;12:469–80.