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Acellular dermal matrix in premature ejaculation
A preliminary study

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Abstract

Background: To investigate the efficacy of acellular dermal matrix in penis augmentation (ADMPA) for premature ejaculation (PE).

Methods: A total of 39 patients treated with ADM in penis augmentation from June 2014 to December 2017 were evaluated. Detailed evaluations on PE were conducted before operation and at the 6-month and 2-year follow-up visits after operation. Self-estimated intravaginal ejaculatory latency time (IELT) and 5-item version of the International Index of Erectile Function (IIEF-5) were used to measure the ejaculation and the erectile function for all subjects.

Results: Compared to the baseline data, the IELT and IIEF-5 scores were increased, and PE was relieved at 6 months and 2 years after operation. No major complications occurred in the series. Minor complications were resolved with conservative treatment within 3 weeks. The psychosexual impact of the operation was beneficial in the majority of cases.

Conclusion: Our survey systematically evaluated the effects of ADMPA for PE. ADMPA might be an optional surgical method in patients with PE, especially for those who seek penile augmentation. However, given the small amount of cases involved in this study, further studies on the effect of ADMPA for PE were still needed.

Abbreviations: ADM = acellular dermal matrix, ADMPA = acellular dermal matrix in penis augmentation, DNP = dorsal nerve of the penis, GPAH = glans penis augmentation by subcutaneous injections of hyaluronic acid gel, HA = hyaluronic acid, IELT = intravaginal ejaculatory latency time, IIEF-5 = 5-item version of the International Index of Erectile Function, PE = premature ejaculation.

Keywords: augmentation, glans penis, hypersensitivity, premature ejaculation

1. Introduction

Men are often worried about the size of their penis and ejaculatory latency time, and sometimes seek enhancement to improve their self-esteem or to satisfy and/or impress their partners.[1] A variety of exogenous materials has been used in procedures to enhance the penile girth, since penile augmentation was reported in the 19th century.[2,3] Allografts in the form of an acellular inert dermal matrix derived from donated human skin tissue have also been used for penile girth. Penile girth enlargement by acellular dermal matrix (ADM) grafts has several advantages over augmentation with autogenous dermis-fat grafts: the elimination of donor site morbidity and a significantly shorter operation time.[4] With this approach, through a short dorsal incision at the base of the penis, the scar is concealed in a crease covered by pubic hair and thus hardly visible. Although a survey conducted by Tealab et al showed that penile augmentation by porcine acellular dermal grafts might negatively affect male sexual status (4 in 18 patients reported decreased penile sensation at 6-month visit),[5] penile enlargement by implantation of ADM was a safe and effective operation in most of the reports[4,6] and, no major complications occurred in the patients received penile augmentation by ADM.[7]

To the best of our knowledge, there were few studies to evaluate the relationships between adult penile augmentation by ADM and premature ejaculation (PE). Therefore, we conducted an observational study to investigate whether there were any relationship between ADMPA and PE.

2. Subjects and methods

2.1. Subjects, inclusion criteria, and exclusion criteria

A total of 39 patients treated with ADM in penis augmentation from June 2014 to December 2017 were evaluated (mean age at the time of surgery was 29 years, range 24–37). The indications for augmentation were the perception of a short penis, seeking more sexual pleasure, or a combination of both.

Inclusion criteria: the age of patients treated with ADMPA was over 18 years; all subjects had not been treated with any penile augmentations prior to ADMPA; all subjects had have a

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Informed consent was obtained from all participants. Permissions for use were received from participants who provided photos.

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heterosexual, stable, and monogamous sexual relationship with the same partner for at least 6 months. In addition, because some subjective questions were asked in our study, eligible men should be able to comprehend and speak Chinese.

Exclusion criteria mainly included deformity of penis, a bleeding disorder, keloid formation, and other conditions that might unduly increase the risks of elective surgery. In addition, men who have used medications that could affect their ejaculatory function were excluded (e.g., selective serotonin reuptake inhibitors and phosphodiesterase type inhibitors).

2.2. Study design and procedure

Prior to the survey, all subjects were informed about the procedure of the survey, and those who participated were asked to provide written consent. The IRB was obtained from Peking University People's Hospital. This survey was designed as a 3-stage protocol.

Firstly, prior to the ADMPA, all subjects were asked to undergo a physical examination by an experienced clinician. Then, all subjects were asked to complete a verbal questionnaire, which included information regarding basic demographic variables (e.g., age and educational and occupational status), medical and sexual histories (e.g., self-estimated intravaginal ejaculatory latency time [IELT], duration of the relationship, and frequency of sexual intercourse), and self-estimated scales (e.g., the Chinese version of International Index of Erectile Function-5 [IIEF-5]).[8] The contents of verbal questionnaire were recorded and assessed by a single physician to exclude interpersonal variation. In addition, based on the PE definition suggested by ISSM,[9–11] men were diagnosed with lifelong PE if they experienced vaginal penetration for <1 minute, a loss of control, and/or negative sexual consequences. The IIEF-5 questionnaire contained 5 questions that were answered according to symptoms (scale range 0–5). IIEF-5 scores ≥22 points were rated as normal erectile function, while scores <22 were rated as erectile dysfunction (ED). The Chinese version of IIEF-5 has been used in Chinese male population in previous studies.[12] The Cronbach alpha coefficients for the Chinese version of IIEF-5 in our survey were 0.79, which indicated acceptable internal consistent reliability. Emotional, psychologic and social factors are excluded by patient reporting before answering the questionnaires. The flaccid girth (Fig. 1A) and erect girth of penis was measured before operation. In the 2nd stage, all men received a penile augmentation with ADM. Briefly, under local or spinal anesthesia, a circumferential subcoronal incision was used for penile degloving. The incision was deepened through the skin, Colles' fascia, and down to Buck fascia, which was preserved. The shaft was then degloved down to the root of the penis. One layer of ADM (10 cm × 10 cm) was incised according to the penis size and then used to wrap around the penile shaft from the coronal sulcus to the root (Fig. 2A and B). These grafts were then sutured to Buck fascia with 4-0 vicryl from the root to coronary sulcus of glans. A pressure bandage was then used to wrap the penis with moderate compression to avoid these grafts' shifting, wound hematoma and edema of penis, exclusively around the shaft (Fig. 2C). Antibiotic prophylaxis began to be used the night before surgery and continued for 1 week after surgery. Patients were instructed not to have sexual intercourse for the first 2 months after surgery. The incision after operation is shown in Figure 3.

The 3rd stage involved 6-month and 2-year follow-up visits. At the visit, all subjects underwent a standardized medical history and physical examination. Then, information on ejaculatory and erectile function was collected by the same physician who conducted the verbal questionnaire using a verbal questionnaire, which mainly concentrated on sexual history, and included the Chinese assessment of IELT and IIEF-5. The flaccid girth (Fig. 1B) and erect girth of penis after operation was measured. Finally, detailed records for all subjects before circumcision and at follow-up visit were entered into the database.

2.3. Statistical analysis

All statistical analyses were performed using the SPSS software (version 13.0; SPSS Inc, Chicago, IL). Descriptive statistics were used to summarize the subjects' characteristics. Data on demographic information for all subjects were expressed as mean ± standard deviation (SD). Data (including self-estimated IELT and IIEF-5 measurements) at baseline (before operation) and 6-month and 2-year follow-up visit for all subjects were expressed as mean ± SD. Data with a normal distribution were evaluated by analysis of variance and paired t test. $P < .05$ was considered to be statistically significant.

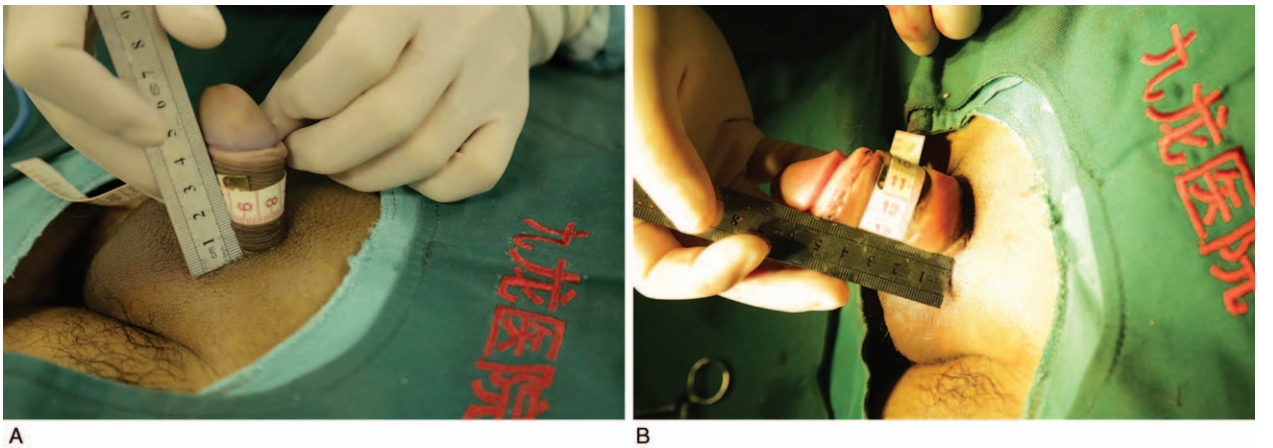

Figure 1. The flaccid girth of penis before and after operation. (A) The flaccid girth before operation. (B) The flaccid girth after operation.

Figure 2. (A) The shaft was degloved down to the root of the penis. (B) ADM was wrapped around the penile shaft and sutured to Buck fascia. (C) The penis was wrapped with a 5-cm pressure bandage after operation.

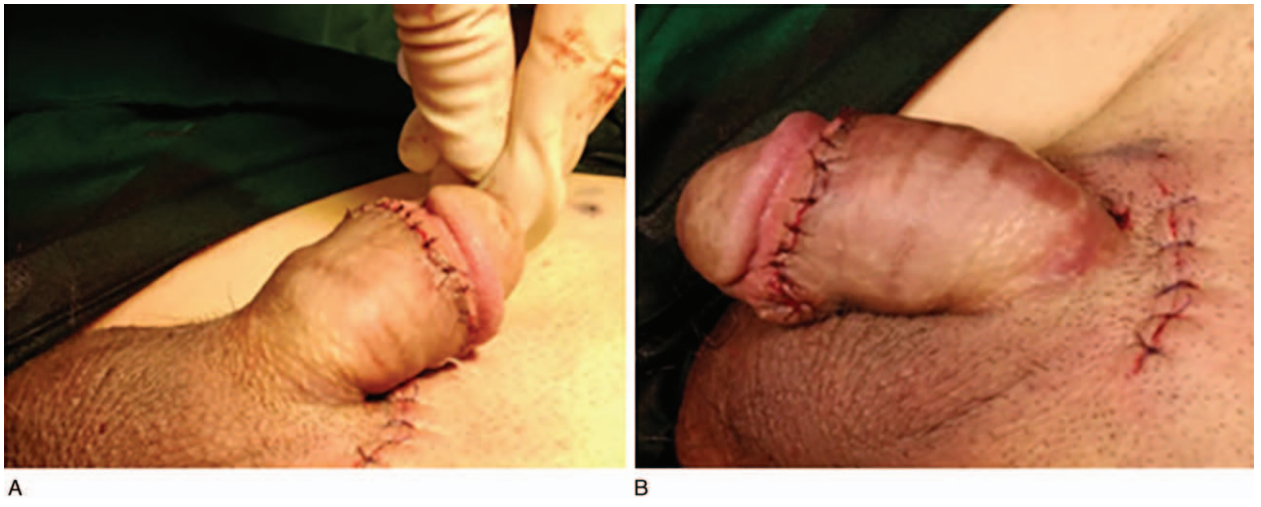

Figure 3. (A) The penis after the completion of penis augmentation operation. (B) The infrapubic incision was made for penile lengthening.

Table 1

Demographic information and sexual status for all subjects prior to operation.

	Age, y	Duration of the relationship, y	Frequency of sexual intercourse, time/4 wks
Preoperation	29.22 ± 3.70	4.56 ± 2.07	7 ± 2.55

3. Results

3.1. Demographic information

Of the 39 patients enrolled in the study, 39 (100%) males completed 6-month and 2-year follow-up. Detailed demographic information for all subjects at baseline is summarized in Table 1.

3.2. Outcomes of penile circumference, IELT, and IIEF-5

As shown in Table 2, the mean flaccid girth and erect girth were 6.93 ± 1.00 cm and 10.59 ± 1.15 cm, respectively; 8.07 ± 1.06 cm and 12.79 ± 1.22 cm at 6 months, respectively; 7.89 ± 1.04 cm and 11.53 ± 1.19 cm at 2 years, respectively. Compared to the baseline (225.6 ± 120.4 seconds and 15.2 ± 3.5), the mean self-estimated IELT and total IIEF-5 scores were increased to 424.3 ± 123.8 seconds and 21.33 ± 2.8 at 6 months, to 412.8 ± 123.1 seconds and 19.6 ± 2.6 at 2 years ($P < .05$). Although the mean flaccid girth, erect girth, self-estimated IELT, and total IIEF-5 score were slightly decreased at 2 years compared to those at 6 months, statistical differences were not observed. No major complications occurred. Although 2 patients developed delayed wound healing, the ADM was not exposed and the 2 patients' wounds healed well after recurrent wound dressing changes for 1 month.

4. Discussion

The PE was a multifactorial disease that might caused by a variety of factors, including biologic and psychologic aspects. Management of PE has evolved tremendously over the last 20 years. Current treatment choice for PE is medical treatment.[13] However, the recurrence after withdrawal of medication is still the main limitation of medical treatment for PE.[14] Patients with primary PE often had penile hypersensitivity, which provided further implications for an organic basis of PE.[15] In hypersensitivity of glans penis, various topical agents were applied, but the efficacies were still controversial.

Surgical treatments to decrease sensation of the glans had demonstrated efficacy on treating PE but were not recommended due to possible sensory loss and rare ED. The major concern of guideline committees was not efficacy but safety. Dorsal neurectomy was also created to decrease the sensitivity of glans penis. Dorsal neurectomy was not an established treatment for penile hypersensitivity ejaculation due to the uncertain pathophysiology, invasiveness, and side effects, for example, numbness paresthesia, pain for neuroma, Peyronie disease, and even ED.[16–18] Despite these limitations, dorsal neurectomy was still performed in selective patients who do not respond to conventional treatment for PE.

Hyaluronic acid (HA) gel glans penis augmentation treating PE had also gained popularity in some Asian country, like South Korea, albeit at a slower rate than dorsal nerve neurectomy.[19] Glans penis augmentation by subcutaneous injections of HA gel was initially developed to augment a small glans penis, but some patients were reported to have PE improvement treated with HA gel.[16] They postulated the theoretical efficacy of glans penis augmentation by subcutaneous injections of HA gel (GPAH) in patients with PE. It neither completely abolished sense of the glans or penis nor caused sexual dysfunction because GPAH did not affect the dorsal nerve, especially the dorsal nerve in the glans. However, the main limitations of GPAH were possible long-term volume loss, unnaturally looking surface, expense of filler, and lack of multicenter studies. Major contributing factors of sensation in glans penis were distribution of dorsal nerve, number of receptor, threshold of receptor, and accessibility of stimuli to the receptor. Therefore, new treatment strategies for PE should be studied to increase the efficacy of treatment on PE and decrease the complications.

The ADM has been used with increased frequency over the last decade to assist during prosthetic breast reconstruction and other reconstructive surgeries.[20–22] ADM was also used for patients with penile augmentation and no major complications occurred in the patients received penile augmentation with ADM.[4,5,7] Alei et al used porcine dermal acellular grafts for penile augmentation in 69 candidates and followed for more than 1 year. They reported a 40% increase in penile girth during flaccidity, and 22% during erection with no major complications.[7]

Results from our survey showed that self-estimated IELT was significantly associated with adult penile augmentation with ADM. At the 6-month and 2-year visits, patients treated with the penile augmentation by ADMPA were with higher self-estimated IELT and total IIEF-5 score compared with that at baseline. In addition, the flaccid girth and erect girth were also increased after treatment with ADMPA. No major complications occurred in the series. Minor complications were resolved with conservative treatment within 3 weeks. Sexual activity was resumed from 2 months after surgery.

Combining with the above parameters such as self-estimated IELT and IIEF-5 questions, we were able to perform a comprehensive analysis of the relationships between adult penile augmentation with ADM and PE. In addition, there were no significant differences at 6-month and 2-year follow-up, which indicated a relative stable efficacy of ADMPA for PE. Therefore, our findings might provide a framework for understanding the effect of penile augmentation with ADM on sexual dysfunction. ADMPA for PE might work in 3 ways. Firstly, ADMPA may take effect in the same way as GPAH. ADMs inhibited the tactic stimuli to reach to receptor. The skin of human phallus was innervated by the dorsal nerve of the penis (DNP), trunk of which was composed of 2 different populations of axons.[18] The 1st group traveling along the dorsal midline and terminating in the glans and the other group of fibers radiated from the main trunk

Table 2

Outcomes of penile circumference, IELT, and IIEF-5 at baseline and follow-up visit.

	Flaccid girth, cm	Erect girth, cm	Self-estimated IELT, s	IIEF-5
Baseline	6.93 ± 1.00	10.59 ± 1.15	225.6 ± 120.4	15.2 ± 3.5
6-mo follow-up	8.07 ± 1.06*	12.79 ± 1.22*	424.3 ± 123.8*	21.3 ± 2.8*
2-y follow-up	7.89 ± 1.04*	11.53 ± 1.19*	412.8 ± 123.1*	19.6 ± 2.6*

Compared to the baseline, the mean flaccid girth, erect girth, self-estimated intravaginal ejaculatory latency time (IELT), and total 5-item version of the International Index of Erectile Function (IIEF-5) score at 6-mo and 2-y follow-up were significantly increased.

* $P < .05$. The differences of parameters between 6 months and 2 years were not significant.

over the lateral and ventral aspects of the penile shaft with branches to the corpus spongiosum and urethra.[23,24] At 1 to 2 cm proximal to the corona glandis, the DNP dorsal trunk divided into 2 to 3 nerve bundles. The DNP and its branches along the shaft run just beneath the skin and fascia, the main branches within the glans are 3 to 6 mm from the epithelial surface. The extent of nerve fibers, including in dorsal neurectomy, was important in postoperative sensory of glans penis.[25] ADMs sutured to Buck fascia might cover the micro-branches of the DNP continuously, which resulted in depression of receptor threshold. Second, ADMPA may decrease the proprioception of penis, especially when the ADM is very thick. As we know, millions of proprioception receptors are located in different parts of human body, such as joint space, skin, inner ear, and so forth.[26] Undoubtedly, proprioception receptors are also located in the penis and deeper layer of the skin.[27,28] These receptors are responsible for pressure difference and temperature change in the sexual intercourse.[29–31] Third, glans penis augmentation could increased self-esteem and self-confidence of patients, which might act positively for PE.[32]

Several limitations of the currently study should be considered. First, the limitation of the present study was relatively few patients, which possibly resulted in a type II statistical error, and thus the results and conclusions must be considered provisional until other studies confirm or refute them. Second, although 6-month and 2-year follow-up visits were conducted in our study, longer follow-up visit (e.g., 5-year follow-up visit) should be performed in future studies. Third, this study was patient oriented and based only on subjective reports. Objective data such as penile biothesiometry should be measured to assess penile sensation in the future studies. Fourth, the subjects in our study were not diagnosed with PE, because we could not assure the efficacy of ADMPA on PE but it was effective and safe for girth augmentation. In next step, we need more patients with PE in future studies to demonstrate the efficacy in these targeted patient populations.

5. Conclusion

With the assessments of IELT and IIEF-5, our survey systematically evaluated the effect of ADMPA on PE in China. It provided a better framework with which to determine their relationships. At 6-month and 2-year follow-up visits, patients treated with ADMPA experienced higher IELT and better scores of control over ejaculation than before. ADMPA was found to be associated with PE and might be an optional surgical method in patients with PE, especially for those who seek penile augmentation.

Author contributions

Data curation: Qing Li, Wenjun Bai.
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Software: Huaqi Yin.
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Validation: Huaqi Yin.
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Writing – review & editing: Xiaowei Zhang, Tao Xu.

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