



## Clinical Application of Allogeneic Human Acellular Dermal Matrix in the Treatment of Penile Hypospadias

Yankai Z<sup>1\*</sup>, Hui-Xin C<sup>2</sup>, Haibing C<sup>2</sup>, Tao W<sup>1</sup>, Zhimou W<sup>2</sup>, Jianfeng S<sup>2</sup> and Yuedong C<sup>1</sup>

<sup>1</sup>Department of Urology, the First Affiliated Hospital of Xiamen University, China

<sup>2</sup>Department of Urology, Zhangzhou Hospital of Traditional Chinese Medicine Affiliated to Fujian University of Traditional Chinese Medicine, China

### Abstract

**Objective:** To investigate the effect of allogeneic Human Acellular Dermal Matrix (HADM) in the treatment of penile hypospadias.

**Methods:** The data from January 2019 to December 2022 were compared 30 cases were treated with Tubularized Incised Plate urethroplasty (TIP), and 28 cases were treated with Tubularized Incised Plate urethroplasty (TIP) + HADM covering for newly treated children with penile hypospadias.

**Results:** There were 6 cases of mild urethral meatus retraction, 8 cases of urethrocutaneous fistula requiring reoperation, and 0 case of urethral stricture after the application of Tubularized incised Plate urethroplasty (TIP). After application of TIP and HADM, 6 cases of urethral meatus retraction, 2 case of urethrocutaneous fistula requiring reoperation, and 0 case of urethral stricture were observed. The incidence of urethrocutaneous fistula requiring reoperation was statistically significant ( $P < 0.05$ ), while There was no significant difference in the incidence of urethral meatus retraction and urethral stricture between the two groups ( $P > 0.05$ ).

**Conclusion:** Allogeneic Human Acellular Dermal Matrix (HADM) as a "protective layer" of the new urethra can effectively reduce the incidence of urine leakage during the operation of penile hypospadias.

**Keywords:** Hypospadias; Allogeneic human acellular dermal matrix; Tubularized incised Plate urethroplasty; Urethrocutaneous fistula

### Introduction

Hypospadias is a common congenital urethral anomaly, with an incidence of hypospadias ranging from about 1:200 to 1:300 in male newborns [1,2]. In recent years, there is a gradual increasing trend. Hypospadias shows three main anatomical abnormalities: 1) abnormal anatomical position of urethral meatus; 2) penile curvature and 3) abnormal distribution of foreskin. According to the location of the urethral meatus, the urethra is divided into four types: 1, penile head type; 2, penile type; 3. scrotal type; 4. the perineum type. Treatment goals for patients with hypospadias are to re-straighten the penis to restore normal sexual function, as well as to have a new urethral meatus distal to the head of the penis. Review in January 2017 to December 2022, the first affiliated hospital of Xiamen University and the Zhangzhou Hospital of Traditional Chinese Medicine treated 58 cases of penis for children with penile hypospadias, according to the intraoperative use of allogeneic decellular dermal matrix (HADM) covering new forming urethra is divided into two groups, and the two groups of clinical treatment effect analysis, reported as follows.

### Methods

#### Clinical data

**General information:** A total of 58 children with primary penile hypospadias admitted to the Department of Urology of the First Affiliated Hospital of Xiamen University and the Department of Urology of Zhangzhou Hospital of Traditional Chinese Medicine from January 2019 to December 2022 were included in the study. **Inclusion criteria:** All the children were primary penile hypospadias (including distal, mid, and proximal) and penile bending was mild to moderate (less than 35 degree).

**Exclusion criteria:** Children with a previous surgical history of a penis. All the children were

### OPEN ACCESS

#### \*Correspondence:

Zeng Yankai. Department of Urology, The First Affiliated Hospital of Xiamen University, Xiamen 361000, China

**Received Date:** 04 Nov 2023

**Accepted Date:** 16 Nov 2023

**Published Date:** 21 Nov 2023

#### Citation:

Yankai Z, Hui-Xin C, Haibing C, Tao W, Zhimou W, Jianfeng S, et al. Clinical Application of Allogeneic Human Acellular Dermal Matrix in the Treatment of Penile Hypospadias. *Ann Plast Reconstr Surg.* 2023; 7(3): 1112.

**Copyright** © 2023 Zeng Yankai. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

treated with primary penile extension + urethroplasty, which was divided into two groups: A and B according to the different surgical methods. In group A, 30 patients underwent TIP with mean age ( $25 \pm 13$ ) months; in group B, 28 patients were treated with TIP + allogeneic Human Acellular Dermal Matrix (HADM) coverage with mean age ( $23 \pm 9$ ) months. The comparison of general data between the two groups ( $P$  value greater than 0.05) was no significantly different and comparable.

**Surgical procedure:** In Group A, the TIP procedure was used, surgical procedure: Under general anesthesia, in the supine position, 5-0 polypropylene non-absorbable suture running through the glans penis as traction. Mark the incision line with a sterile marker pen. Circumscribing incision preserved urethral plate. After degloving, the surgeon separates the glans wings from the urethral plate. Corpus spongiosum is dissected from the cavernosal bodies and released distally from the glans wings for later spongioplasty. Artificial erection is performed, and if curvature is less than 30 degrees and corrected with plication, TIP procedure can be considered. Midline urethral plate incision, extended to the level of the corporal bodies. Two-layer urethral plate tubularization using interrupted subepithelial 7-0 polyglactin suture. Spongioplasty approximates divergent corpus spongiosum over the neourethra before a tunica vaginalis barrier flap is added. Proper dressing of the transferred dorsal foreskin, cover with the penis. Shear side hole of silicone tube. After adjusting the position and being fixed to the glans penis, using Vaseline gauze, sterile gauze, elastic self-adhesive bandage, we remove and dressing 5 days after operation. From 10 to 12 days after operation, we remove the silicone tube.

Group B using TIP + allogeneic Human Acellular Dermal Matrix (HADM) cover, surgical procedure: TIP (Group A surgical procedure), select suitable for acellular dermal stromal slice and cut, cut the newly forming urethra and fixed in the penile cavernosum membrane number needles (Group A).

**Statistical methods:** Using SPSS 22.0 statistical software for data analysis with  $\bar{x} \pm s$ , independent sample  $t$  test, count data with relative number and binomial distribution test.  $P < 0.05$  was considered as a statistically significant difference.

## Results

In Group A, 6 cases were the mild retraction of urethral meatus, 8 cases of urethrocutaneous fistula requiring reoperation, and 0 cases of urethrostenosis; in Group B, 6 cases were the mild retraction of urethral meatus; 2 cases of reoperation (4 cases of urethrocutaneous fistula after urethral stent removal, allogeneic acellular dermal

matrix covering new urethra, after 1 to 2 weeks of dressing, 2 cases of urine leakage stopped and fistula healed, and the other 2 cases had continuous urine leakage and reoperation for repairing of the urethrocutaneous fistula). The incidence of urethrocutaneous fistula requiring reoperation was statistically significant ( $P=0.010 < 0.05$ ), and the incidence of mild retraction of urethral meatus ( $P=1 > 0.05$ ) (Table 1, 2).

## Discussion

Hypospadias is a common congenital malformation of pediatric genitourinary system. Many factors may participate in this mechanism, such as endocrine disorders, genetic defects, environmental factors and so on. Hypospadias not only brings the dysfunction of urination and reproductive function to children, but also affects the psychological development of children, causing great family pressure, improves the cure rate of hypospadias, and reduces postoperative complications, which is of great significance to both patients and society. Surgical treatment is still the only means of hypospadias. What the current concept holds is that hypospadias deformity should be corrected before the child can feel his birth defects, so as to prevent his self-image and emotional development from being adversely affected. The literature believes that the best age for repair is 6 to 18 months [3,4].

More than 300 hypospadias repairs have been reported to date, however, none of these techniques are considered the gold standard [5,6]. The procedure depends on the location of the urethral meatus, the complexity of the repair, technical modifications, and the experience of the surgeon [7-10]. Current treatment of patients with hypospadias of penile size, in addition to the classic transverse pedicle island prepuce flap surgery (Duckett procedure), There are also urethral orifice basal flap capping (Mathieu procedure), pedicled island flap capping (Onlay island flap procedure), Tubularized Incised Plate urethroplasty (TIP), also known as the Snodgrass procedure. Where the TIP procedure is from the Snodgrass [11]. In 1994 and proposed in the treatment of hypospadias, this procedure was widely used in clinical practice and achieved satisfactory efficacy and prognosis. Because of the advantages of convenient materials, simple procedure and less complications, it has become one of the common procedures for the treatment of hypospadias [12-14]. From the perspective of the surgical repair of the hypospadias, urethroplasty is the most critical and difficult step throughout the treatment process, and is the main direction of the current research, but regardless of the method of repairing hypospadias, some postoperative complications occurred such as urethral meatus retraction and Urethrocutaneous Fistula (UCF), urethrostenosis, urethral diverticulum and recurrence

**Table 1:** Comparison of the general information of the children.

Groups	Age (month)	Ventral penile curvature (degree)	Urethral defect length (cm)	Follow-up time (months)
A group	$25 \pm 13$	$18.6 \pm 9.5$	$1.85 \pm 0.63$	$5.8 \pm 3.5$
B group	$23 \pm 9$	$17.8 \pm 8.1$	$1.79 \pm 0.51$	$5.6 \pm 3.1$
t value	2.086	1.376	1.526	1.275
p value	0.0925	0.285	0.2251	0.3335

**Table 2:** Comparison of the postoperative complications.

Groups	Recurrence of ventral penile curvature	urethrostenosis	Mild retraction of urethral meatus	Reoperation for Urethrocutaneous Fistula
Group A (30 patients)	0 cases	0 cases	6 cases	8 cases
Group B (28 patients)	0 cases	0 cases	6 cases	2 cases
P value			1.000	0.010

of ventral penile curvature. Among them, UCF is one of the most common complications following hypospadias repair, the incidence of UCF after hypospadias. The current recognized incidence rates range from 15% to 30%, even though the surgeon is skilled. Its incidence is also from 5% to 10% [15], this complication remains a frustrating and challenging problem to date, with local infection, ischemia, edema, wound dehiscence, intraoperative manipulation and improper tissue handling considered contributing to cause this complication [16,17]. UCF often requires another corrective operation, which increases the risk of surgical and anesthetic complications, as well as the potential financial and psychological burden, and how to reduce the incidence of UCF is of great significance to both surgeons and patients.

It has been reported in the literature that the insertion of an additional barrier layer, namely the covering material, between the newly formed urethra and the skin during hypospadias repair, can effectively reduce the incidence of UCF [18,19]. In the past, the covering materials commonly used in clinical practice came from autologous materials, including: The superficial subcutaneous fascia flap of prepuce and scrotum, namely Dartos fascia flap, de-epithelialization flap, cavernosal tissue, testicular sheath flap, external fascia flap with pedicled sperm cord, etc. Because children with hypospadias often associated with penis skin dysplasia or previous surgical history, and excessive separation of foreskin subcutaneous fascia, may lead to skin ischemia necrosis, resulting in surgical failure, and the distal autograft acquisition brings additional risk of postoperative pain and complications, thus affecting the use of autologous materials. This prompted the search for a covering material that can provide similar wound healing support, and for all patients, so bioCs (BAUCs) have three main types: Acellular Matrix (AM), Tissue Adhesive (TAs) and autologous Platelet-Rich Plasma or Fibrin (PRP/PRF).

The Bio-Assisted Urethral Coverings (BAUCs) used in this study were Acellular Dermal Matrix (ADM). ADM is divided into two categories: Heterogeneous and heterogeneous ADM (pig source ADM and cattle source ADM). Characteristics of the same ADM are as follows: 1. Take from healthy human skin tissue; 2. Keep extracellular matrix morphology, 3D structure and composition; 3. It can induce the patient's own cells to enter, make body damage and missing tissue rapid repair; 4. No bacterial growth, no toxicity, no irritation, no obvious immune rejection; 5. Better tissue compatibility; 6. Small foreign body reaction. Studies have shown that the same ADM is not replaced by the host tissue after implantation and allows its own tissue to grow into it, thus replacing the absent or atrophic own tissue. In the early stage of implantation, due to its porous nature, the nutrition of the graft has no impact, and the lack of cellular components will not cause cell necrosis and inflammation due to metabolic disorders caused by insufficient blood supply to cells. In the later stage, due to the particularity of the production process, the residual extracellular matrix structure can promote the rapid growth of blood vessels in the transplantation material, so it is more reasonable and better than its own tissue.

In this study, the use of allogenic ADM to cover the newly formed urethra group could effectively reduce the incidence of UCF, and the incidence of mild retraction in the urethral meatus and the incidence of urethrostenosis were not statistically significant. Four patients had developed urethrocutaneous fistula after the removal of the urethral stent tube. Allogeneic human acellular dermal matrix exposed covering the new urethra, however, in two cases, the urinary leakage was stopped after 1 to 2 weeks of dressing change treatment, the fistula is healing.

This indicates that consume ADM has good efficacy in the repairing and reconstruction of local tissue defects. Its mechanism of action is related to its biological characteristics. Allogeneic ADM is allogeneic skin tissue treated by biochemistry and biological tissue engineering technology. Removal of the epidermis, and acellularization, retaining the collagen, elastic fibers in the extracellular matrix are required. With a three-dimensional stereo structure, host cells grow in scaffold adhesion after patient implantation. Secreting of a new extracellular matrix, it forms its own organization, thus to complete the local tissue repair and reconstruction. Allogeneic ADM minimally reduces host immune rejection with better histocompatibility. In addition, in this study in Group A, the single layer covered the newly formed urethra, and in Group B, the same ADM + ventral subcutaneous fascia was used to cover the newly formed urethra, which may also be one of the reasons for the reduced incidence of postoperative UCF in Group B. A foreign meta-analysis shows that [20] the use of Bio-Assisted Urethral Coverages (BAUCs) may reduce the incidence of UCF after hypospadias, and the fascia flap with BAUCs + Dartos seems compared to BAUCs alone, supporting the principle that more layers are better.

All in all, despite the continuously improved techniques of hypospadias repair, the formation of postoperative UCF remains a significant challenge. Allogeneic Acellular Dermal Matrix (ADM) as the "protective layer" of the newly formed urethra can effectively reduce the incidence of UCF after penile hypospadias surgery, and does not increase the incidence of urethral retraction and urethral stricture, and Acellular Dermal Matrix (ADM) has good histocompatibility and no rejection, has good efficacy in the repair and reconstruction of local tissue defects, and can be widely used in clinical practice. Given the small sample size and was conducted at a single institution, more clinical study data and rigorous prospective evaluation are needed to validate this benefit.

## References

- Gopal SC, Gangopadhyay AN, Mohan TV, Upadhyaya VD, Pandey A, Upadhyaya A, et al. Use of fibrin glue in preventing urethrocutaneous fistula after hypospadias repair. *J Pediatr Surg*. 2008;43(10):1869-72.
- Schnack TH, Poulsen G, Myrup C, Wohlfahrt J, Melbye M. Familial coaggregation of cryptorchidism, hypospadias, and testicular germ cell cancer: A nationwide cohort study. *J Natl Cancer Inst*. 2010;102(3):187-92.
- Nan L, Chunquan C. Etiology and current diagnosis and treatment of hypospadias. *J Tianjin Med University*. 2022;28(1):108-111.
- Linlin Z, Mingjie W. Surgical treatment of hypospadias and its new progress. *J Modern Urol*. 2023;28(2):93-6.
- Keays MA, Dave S. Current hypospadias management: Diagnosis, surgical management, and long-term patient-centered outcomes. *Can Urol Assoc J*. 2017;11(1-2 Suppl 1):S48-S53.
- Snodgrass W, Bush N. Primary hypospadias repair techniques: A review of the evidence. *Urol Ann*. 2016;8(6):403-8.
- Baskin LS, Ebberts MB. Hypospadias: Anatomy, etiology, and technique. *J Pediatr Surg*. 2006;41(3):463-72.
- Van der Horst HJ, De Wall LL. Hypospadias, all there is to know. *Eur J Pediatr*. 2017;176(4):435-41.
- Appeadu-Mensah W, Hesse AA, Glover-Addy H, Osei-Nketiah S, Etwire V, Sarpong PA. Complications of hypospadias surgery: Experience in a tertiary hospital of a developing country. *Afr J Paediatr Surg*. 2015;12(4):211-6.
- Subramaniam R, Spinoit AF, Hoebek P. Hypospadias repair: An overview

- of the actual techniques. *Semin Plast Surg.* 2011;25(3):206-12.
11. Snodgrass W. Tubularized, incised plate urethroplasty for penile hypospadias. *J Urol.* 1994;151(2):464-5.
  12. Steven L, Cherian A, Yankvic F, et al. Current practice in paediatric hypospadias surgery; A specialist survey. *Pediatr Urol.* 2013;9(6):1126-30.
  13. Springer A, Ktois W, Horcher E. Trends in hypospadias surgery: Results of a worldwide survey. *Eur Urol.* 2011;60(6):1184-9.
  14. Qiao L, Jinyu C, Yifan Z. Effect of modified urethral plate longitudinal method in the treatment of pediatric hypospadias. *Contemporary Med China.* 2019;6(15):103-5.
  15. Urology Group, Pediatric Surgery Branch of Chinese Medical Association. Expert consensus on hypospadias. *Chinese J Pediatr Surg.* 2018;39(12):883-8.
  16. Shenoy NS, Tiwari C, Gandhi S, Kumbhar V, Joseph V, Basu S, et al. Efficacy of fibrin sealant as waterproof cover in improving outcome in hypospadias surgery. *Afr J Paediatr Surg.* 2020;18(4):215-8.
  17. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *Int J Surg.* 2021;88:105906.
  18. Fahmy O, Khairul-Asri MG, Schwentner C, Schubert T, Stenzl A, Zahran MH, et al. Algorithm for optimal urethral coverage in hypospadias and fistula repair: A systematic review. *Eur Urol.* 2016;70(2):293-8.
  19. Lugang H, Weiping Z. Rethink the application of longitudinal resection ureplasty of urethral plate. *J Clin Pediatr Surg.* 2020;19(12):1061-5.
  20. George WM, Jane TK, Christina PC. Biologic adjuvant urethral coverings for single-stage primary hypospadias repairs: A systematic review and pooled proportional meta-analysis of postoperative urethrocutaneous fistulas. *J Pediatr Urol.* 2022;18:598-608.