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REVIEW

The Extended Utilization of Bulking Agents in Pediatric Urology

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Abstract

Purpose of Review Traditional surgical management for urinary incontinence and vesicoureteral reflux often requires complex reconstructive surgery and extended hospitalizations. Since the introduction of endoscopic bulking agents in 1973, there has been increasing interest in the use of endoscopic injection (EI) and bulking for the treatment of a variety of pediatric urologic disorders. The purpose of this review is to summarize the most recent literature addressing the use of bulking agents in pediatric urology.

Recent Findings The most recent literature has focused primarily on the use of EI of bulking agents at the bladder neck for the treatment of urinary incontinence. Other uses of EI of bulking agents has focused on the treatment of vesicoureteral reflux (VUR) in patients with anatomic abnormalities or treatment of incontinence catheterizable channels.

Summary The development of advanced techniques for endoscopic injection along with safe, stable bulking agents has allowed for the treatment of a variety of urologic conditions. This minimally invasive procedure offers an additional tool for the pediatric urologist's armamentarium in the treatment of urinary incontinence and VUR.

Keywords Bulking agents · Endoscopic injection · Pediatric urology

Introduction

Traditional surgical management for urinary incontinence (UI) and vesicoureteral reflux (VUR) involves complex reconstruction and extended hospitalizations. While the introduction of enhanced recovery methods and minimally invasive surgical procedures has lessened the burden of these procedures, endoscopic interventions for the treatment of these conditions offers a truly minimally invasive option for patients. The concept of endoscopic injection (EI) of the bladder neck for treatment of urinary incontinence (UI) is over 50 years old. In 1973, Berg described the use of a polytetrafluoroethylene (Teflon©) as a bladder neck bulking agent for 3 patients with good success [1]. Following this success, endoscopic injection of bulking agents for treatment of primary vesicoureteral reflux (VUR) was described by Matouschek in 1981 using the same Teflon© paste [2]. Since these initial descriptions, several bulking agents, techniques, and applications have been attempted to find the safest, most efficacious methods for the treatment of a variety of urologic conditions.

Bulking Agents

Since Berg's description of endoscopic injection for urinary incontinence, there has been ongoing research for the optimal injectable agent. While initial reports have high success rates utilizing Teflon©, it has since fallen out of favor due to concerns about migration to distant sites including the brain [3], as well as local granulomatous reaction [4]. Glutaraldehyde cross-linked bovine collagen presented another possibility, given its easy injectability and mild host inflammatory response. However, long-term results with collagen injection for treatment of VUR proved to have poor durability and host responses with immunologic responses such as allergic reactions and development of connective-tissue diseases following collagen injection [5]. Polydimethylsiloxan (Macroplastique©), is a silicone elastomer made up of a combination of polydimethylsiloxane and a carrier gel, with an average particle diameter of 209μm, with a range of particle sizes from 34 to 540μm. Unfortunately, the presence of particle sizes below 80μm increases the possibility

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of particle migration, although to date no *in-vivo* studies have demonstrated this concern. Dextranomer/hyaluronic acid (Deflux©), was introduced in 1995, and is made up of dextranomer microspheres, sized 80-100μm, suspended in a carrier gel of hyaluronic acid. Given the large size of the microspheres and the non-immunogenic nature of the carrier hyaluronic acid, Deflux© represents an extremely safe and effective bulking agent that is easily injected. Comparisons between Deflux© and Macroplastique© have shown no significant differences in outcomes for VUR [6], but given the relatively safer profile of Deflux©, it has been widely accepted as the agent of choice for endoscopic bulking procedures.

Bladder Neck Bulking for Urinary Incontinence

Short and Long Term Success in Endoscopic Injection

Early insights into incontinence management show promising results: Dean et al. in 2007 reported their results of endoscopic bladder neck injection with Deflux© of which 82% had incontinence secondary to neurogenic bladder. 71% of patients achieved social continence at 3 months follow-up and 79% of patients that were seen on long term follow up (11.7 months on average)reported symptomatic improvement. They also reported a 43% completely dry rate at an average of 11 months, but this study suffered from almost half of all patients being lost to follow up before long-term efficacy could be assessed [7].

Dyer et al. examined bulking with either Teflon© or Deflux© from a cohort that underwent EI for UI, excluding any patients with previous bladder neck surgery defined as bladder neck sling, artificial urinary sphincter placement, or bladder neck reconstruction. They found differences between success rates related to the etiology of UI: children with UI due to exstrophy/epispadias had no improvements in UI while those with spinal dysraphism experienced moderate success: one two children were dry at 6 months while two others had initial success but failed after 6 months. No differences in success rates between Teflon© and Deflux© were identified, but the study authors did note a need for increased volumes of Deflux© used for injection and rates of continence: all patients considered "dry" were injected with between 4-10cc of bulking agent [8]. Conversely, another study found no association between injected volume and outcomes [9], as they reported on patients undergoing EI following failed bladder neck slings an initial continence rate of 38% which dropped to 23% after long term follow up at 39 months. These patients had previously undergone bladder neck surgery for incontinence due to neurogenic bladder. The authors also noted that in cases of failed EI, on second injection, "the prior injected material was either not visible, or appeared to have less volume and/or be shifted from the bladder outlet" suggesting that the etiology of failure may be due to local migration or molding of the bulking agent.

Pakkasjarvi and Taskinen sought to determine if intraoperative success of endoscopic injection, defined as increased abdominal leak point pressure (ALPP), could predict the long-term outcome in the treatment of urethral sphincter insufficiency, finding no significant correlation. ALPP was measured intraoperatively using a suprapubic tube and manometer with manual compression of a half-full bladder. Examining a heterogenous group of patients with both neurogenic and non-neurogenic bladders as well as various histories of bladder neck procedures, the study noted a median increase in intraoperative ALPP from 19 to 70 ($p < 0.001$), yet this did not reliably predict clinical treatment success, suggesting that intraoperative metrics may not fully capture the complexity of achieving continence and the authors noted that, as has been seen before, the duration of effect on continence was short, lasting an average of 8 months [10]. This short duration of effect was confirmed with a more homogenous population by Stout and colleagues. They report that in patients undergoing EI with Deflux© following a failed bladder neck surgery, only 16% of patients were dry at 6 months [11].

Large studies of bladder neck injection are marred by a heterogenous mix of etiologies for UI. A study by Alova et al., reviewed the outcomes of continence procedures after failed Deflux© treatment, for patients with UI due to exstrophy/epispadias, neurogenic bladder, defunctionalized bladders due to bilateral ectopic ureters and others, reporting that 41% of patients were dry, and 19% significantly improved at 12 months follow-up [12]. This study also examined the outcomes of secondary continence procedures such as bladder neck reconstruction or slings, reporting that injection of bladder neck bulking agents does not affect the success rates of more invasive options following EI. Guys et al. in 2006 performed a sub-analysis and compared success rates in patients undergoing EI with UI due to neurogenic bladder or exstrophy/epispadias and found no significant differences in success rates between the two groups at long term follow up, reporting a constant rate of dryness or improved continence between 4 and 7 years of follow up [13]. A similar, large study of 58 patients found no differences in success rates on multivariable analysis at a median follow up of 6.4 years, for any patient or disease characteristic in a heterogeneous group of patients with male epispadias, female epispadias, and classic bladder exstrophy [14].

In patients with exstrophy/epispadias complex, those who had partial continence, daytime dry intervals of 1 to 3 h, saw a durable increase in social continence, a daytime dry interval of greater than 3 h, with a 63% success rate. This

success was less profound in those patients who began with complete incontinence however, with only a 13% success rate. Finally, success rates of EI were significantly associated with higher pre-intervention bladder capacities in the entire cohort [15]. These results suggest that continence rates can be improved with careful patient selection.

Technique Variability and Patient Selection

The optimal technique for EI for bladder neck bulking has yet to be established, and the techniques described in the current literature are broad. In patients that have continent catheterizable channels (CCC), the technique is often an antegrade approach with retrograde approaches being utilized for an inability to reach the bladder neck or for poor visualization [7, 9, 12, 16–18] Other studies utilized an only retrograde approach [10, 15, 19]. Methods for bladder drainage were also variable, with some studies commencing normal CIC or foley catheterization per urethra immediately after EI [16], while others utilized bladder rest via a suprapubic catheter or catheter in the CCC for several days after EI [17]. One study in which catheterization per urethra was avoided for 2 weeks reported an 80% success rate with Deflux© injection of the bladder neck at 12 months of follow-up. Of note, no patient within this group had prior bladder neck surgery or CCC creation, and all had normal bladder compliance.

Fiorenza et al. reported an increased rate of success of bladder neck injection in patients with UI associated with male epispadias, with a 70% success rate, while female epispadias and bladder exstrophy patients had a an approximately 45% success rate. Univariable analysis showed that male epispadias patients had significantly higher success, but this association disappeared on multivariable analysis. These data however suggest that careful patient selection may have an effect on outcomes, and larger, multi-institutional studies should further examine this association and stratify patients based on eitology of UI as well as prior surgical history [14].

Comparative Efficacy of Bulking Agents

Eftekharzadeh et al. compared the bulking effect of calcium hydroxyapatite and Deflux© in the bladder neck for improving UI in bladder exstrophy-epispadias complex, finding no significant difference in continence rates between the two agents [19]. Other studies have examined the efficacy of different bulking agents and found no association with improved continence rates. Bulking agents examined were Teflon©, Macroplastique©, cross-linked Bovine collagen, and Deflux©. Given the move away from Teflon© and Macroplastique©, Deflux© has become the primary injectable bulking agent, however more recently developed agents such as polyacrylamide gel (Bulkamid©) have had success in the treatment of non-neurogenic SUI in older adults and may be of value for further investigation [20, 21]. Overall, the stable success rates across studies suggest that the choice of bulking agent may be less critical than previously assumed, with technique and patient selection possibly playing more significant roles in outcome success.

Future Directions

The treatment of urinary incontinence with bladder neck bulking agents represents a critical area of urological practice, offering hope for patients with conditions traditionally challenging to manage while maintaining a minimally invasive approach. The specifics and numbers drawn from the key studies illuminate both the potential and the limitations of these interventions. Success in treating UI with bulking agents varies widely, influenced by factors such as patient selection, underlying pathology, and the technique used.

Studies from the last 5 years are relatively sparse and those studies that do exist draw on small and heterogeneous populations. As the field evolves, a more nuanced understanding of these factors, combined with advancements in materials and techniques, may improve the efficacy and durability of bladder neck bulking procedures, ultimately enhancing patient outcomes. To that end, future research should be directed at developing standardized protocols including definitions of success, technical approaches for injection, endpoints for what is considered a successful procedure, post-procedural care, and follow up intervals. Studies should focus on multi-institutional collaboration to allow for larger sample sizes while stratifying patients by etiology of incontinence as well as previous surgical histories. Endoscopic Injection for the Treatment of Vesicoureteral Reflux Associated with Anatomic and Functional Abnormalities.

Treatment of Duplex Ureters, Atrophic Kidneys, and Paraureteral Diverticula

The management of vesicoureteral reflux in pediatric patients, especially those with complex urological anomalies such as duplex ureters, small kidneys, or paraureteral diverticula, presents a significant clinical challenge. The advent of endoscopic injection techniques with the use of Deflux© has offered a minimally invasive alternative to traditional surgical approaches. Additional refinement of techniques and the progression of injection from subureteral Teflon injection (STING) to single and double hydrodistension implantation techniques (HIT) [22] has allowed for increased efficacy in the treatment of VUR. Early studies examined VUR associated with either duplex ureters or small kidneys utilizing the STING technique. In an early study utilizing STING technique in 68 patients and 95% of patients having dilated

VUR, nearly 63% of patients with duplex systems had grade 0 or 1 VUR on VCUG performed 12 months post injection [23]. A larger study using both STING and HIT techniques in 123 patients treated for either UTI, VUR found on sibling screening, or unresolved hydronephrosis associated with duplicated ureters and dilating VUR examined VUR resolution at 3 months with VCUG. The authors found duplicated ureters treated with Deflux© resulted in VUR resolution at 3 months in 68.4% of patients after 1 EI and 94.1% resolution rate after 2 or fewer injections. Single HIT was utilized in all patients with grade 5 VUR and 90% of patients with grade 4 VUR. STING was used in all patients with grade 3 reflux [24]. All children in the study underwent VCUG at 3 months and had subsequent renal and bladder ultrasounds every 2 years with a mean follow up of 6.7 years. Interestingly, the authors of this study also injected both ureteral orifices on the side of VUR regardless of which moiety was refluxing. This may have contributed to the high success rates in the study as injection of a single ureteral orifice can at time cause the second orifice to tent open resulting in secondary reflux. Of note, the one complication reported has immediate post operative gross hematuria lasting 8 h—no cases of obstruction were reported.

In the case of a poorly functioning kidney, one study has examined the efficacy of Deflux©. Lackgren and colleagues identified 40 patients with febrile UTI and VUR demonstrated on 2 VCUGs 6 months apart with associated decreased unilateral kidney function, contributing 10–35% of total function [23]. In these 40 patients, 95% had dilated VUR. The success rate was 70%, irrespective of the grade of reflux. Again, this study utilized the STING technique for injection and while no further studies have examined the efficacy of Deflux© in poorly functioning renal units, this success rate may approach more contemporary success rates with the application of double HIT. Additionally, no decreases in renal function were observed over the course of the study.

Paraureteral diverticula (PUD) represent a structural abnormality of the ureter and bladder wall, but due to size and location may cause abnormal placement or function of injectable bulking agents. In a study by Cerwinka et al. examining patients who underwent VCUG and VUR treatment for breakthrough febrile UTI, persistent VUR after 2 years of observation, new renal scarring or poor compliance with antibiotic prophylaxis; PUD was found in 2.3% of patients. Of these patients with PUD, 50% had dilated VUR. Deflux© injection in patients with PUD had an 81% success rate following a single injection of the ureter on VCUG performed 1–3 months post-operatively. There was also significant association between EI failure injected volume (mean of 1.1cc for failure and 1.7 for success) and the ratio of PUD size to ureteral orifice size, with all ureters having a PUD to ureteral diameter ratio greater than 2.6 resulting in failure. No association was found between failure rates and VUR grade [25]. This study underscores the effectiveness of Deflux© and minimally invasive EI in treating VUR even in the presence of anatomical complexities.

The role of Deflux© has also been investigated for patients with VUR following renal transplantation, with rates of VUR resolution reported between 0 and 64% [26–28]. The first published endoscopic correction of VUR was performed by Williams et al. in 2008, and reported a 43% success rate [28]. Unfortunately no statistical analysis was performed to understand the effect of ureteral orifice placement and VUR grade on the success of Deflux© injection. Similarly, a 2010 study performed with a slightly larger population of 11 patients, all of whom underwent an extravesical Lich-Gregior ureteral reimplant, found a slightly higher success rate of 54.5%, but was unable to identify any characteristics associated with successful treatment of VUR [29]. Castagnetti et al. reported a 64% success rate with Deflux© injection for extravesically reimplanted transplant ureters, and found that etiology of the patient's end stage kidney disease (ESKD) was associated with successful correction of VUR. All cases of ESKD due to upper tract pathology were successfully treated, while injection in patients with ESKD due to lower tract pathology only had a 20% success rate [27]. Ureteral obstruction remains a large concern for transplant patients, and obstruction rates range from 0–33%. Cambareri et al. reported a 23.5% obstruction rate when performing the injection as a STING procedure as well as injecting circumferentially around the ureteral orifice, and injected between 1.6-3ml of Deflux© [30]. A second study that performed a similar injection technique and had similar injected volumes reported a 33% obstruction rate [31]—neither study looked for characteristics associated with obstruction. Given the relative rarity of VUR associated with renal transplantation in children, these studies are plagued with heterogeneity and low sample sizes.

Future Directions

Given the considerable changes to technique for injection of Deflux© for VUR, future studies should examine the role of single and double HIT on success rates for correction of VUR in anatomically complex patients. The use of standardized protocols and operative techniques can allow for objective assessment of predictors of success as well as optimal volumes of Deflux© for injection. Given the relative rarity of these complex anatomic variants, a multicenter approach would be ideal to recruit the large number of patients required to identify prognostic factors. Collectively, these studies underscore the versatility and efficacy of EI with Deflux© in managing a range of complex vesicoureteral reflux. EI with Deflux© is a useful tool in the pediatric urologists' armamentarium, by adjusting injection

techniques, may be able to increase success to near more invasive alternatives while minimizing the risk of morbidity related to open surgery.

Endoscopic Injection for the Treatment of Incontinent Catheterizable Channels

The creation of a continent catheterizable channel by utilizing an appendiceal conduit was first introduced by Paul Mitrofanoff in 1976 [32]. Later adaptations, such as the Yang-Monti technique, for patients with an absent or inadequate appendix were developed and popularized. Further application of the appendiceal conduit resulted in the creating a catheterizable colonic stoma was described by Malone in 1990 [33]. These two procedures are integral in the treatment of patients with spinal dysraphism and its associated neurogenic bladder and bowel dysfunction.

Incontinence rates for urinary CCC range from 10–50%, and revision of a leaking stoma often relies on open revision either at the level of the skin or the valve mechanism at the level of the bladder. Attempts to treat an incontinent catheterizable channel have examined use of EI with Deflux© as a minimally invasive alternative to channel revision. Techniques utilizing an antegrade approach through the stoma for injection and 10–14 days of channel rest with placement of an indwelling urethral or suprapubic tube injection resulted in a 71% success rate after a single EI [34] in carefully selected patients with adequate storage pressures on urodnyamic testing. A second study in similarly selected patients, examining EI of the CCC in a retrograde approach and immediate resumption of channel catheterization, successful EI of Deflux© occurred in only 20% of patients, and a second injection increased the success rate to near 75% [18]. Furthermore, in comparing bulking agents, there was no difference in success outcomes between EI with Teflon©, cross-linked bovine collagen, or Deflux©. Additionally, there appears to be no difference with rates of continence for Bulkamid© and Macroplastique © with each having Mitrofanoff continence rates of 9% [35].

Patient selection may also play a key role in optimizing outcomes. When examining types of channels and reservoirs, patients with appendiceal channels and colonic reservoirs had higher rates of continence following EI than patients with Monti channels and ileal reservoirs [36]. Additionally, there is suggestion that injection of the bulking agent at a specific site, such as the valve mechanism, may increase efficacy of EI. These disparate outcomes following a single injection to an incontinent catheterizable channel suggests that operative technique is essential for a successful outcome.

MACE channels are essential in the treatment of patients with intractable constipation, and leaking MACE channels, while relatively rare, result in significantly decreased quality of life and decreased patient satisfaction [37]. Treatment of a leaking MACE is typically performed with open revision, and few studies have examined the feasibility of EI of MACE with bulking agents. A single review of 9 patients found that after an average of 2 EI procedures, improved MACE continence was achieved in all patients. Unfortunately, this response was not durable, and only 38% of patients reported improved ACE continence at 2 months.. Of note, patients in this series had a 10-12F catheter placed into the MACE which was kept in place for 4–7 days [37]. Similar to the bladder neck bulking procedures, further investigation into the optimal technique and post operative care is needed to understand how to maximize outcomes after bulking injection for CCC and MACE channels.

Conclusion

The evolution of endoscopic injection techniques and the diversification of bulking agents have significantly advanced the treatment landscape for urinary incontinence and vesicoureteral reflux in pediatric urology. The evolution from the use of Teflon© to the contemporary preference for materials like Deflux© underscores a relentless pursuit of safety, efficacy, and minimally invasive management options for these patients. While the quest for the optimal bulking agent continues, the emergence of Deflux© as a favored choice highlights the importance of balancing treatment effectiveness with the potential for adverse reactions and the need for long-term durability.

This review reveals a nuanced understanding of how patient selection, underlying pathology, and technique intricacies play pivotal roles in the success of EI for UI and VUR. Despite the promising strides made in this domain, the variability in outcomes and the transient nature of treatment success call for ongoing scrutiny and refinement of these interventions. However, a minimally invasive procedure that may offer a relatively lower success is often a preferred option for many patients and families.

Moving forward, the integration of multi-institutional collaborations and the standardization of procedural protocols will be crucial in overcoming the limitations posed by small, heterogeneous study populations. This concerted effort will not only pave the way for a deeper understanding of the factors influencing treatment outcomes but also foster innovations that could redefine the therapeutic landscape. Ultimately, the goal remains to offer safe, effective, and minimally invasive treatment options that address the complex needs of this population.

Author Contributions CW and AK contributed equally to the preparation of the manuscript. All authors reviewed the manuscript.

Data Availability No datasets were generated or analysed during the current study

Compliance with Ethical Standards

Conflict of Interest CW has no competing interests. AK is a consultant for Intuitive Surgical, Palette Life Sciences, Teleflex, and Global Continence Inc.

Human and Animal Rights and Informed Consent All reported studies/experiments with human or animal subjects performed by the authors were performed in accordance with all applicable ethical standards including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines.

References

1. Berg S. Polytef augmentation urethroplasty: correction of surgically incurable urinary incontinence by injection technique. Arch Surg. 1973;107(3):379–81. https://doi.org/10.1001/archsurg.1973.01350210017006.
2. Matouschek E. Treatment of vesicorenal reflux by transurethral teflon-injection (author's transl). Urologe A. 1981;20(5):263–4.
3. Aaronson IA, Rames RA, Greene WB, Walsh LG, Hasal UA, Garen PD. Endoscopic treatment of reflux: migration of teflon to the lungs and brain. Eur Urol. 2017;23(3):394–9. https://doi.org/10.1159/000474637.
4. Malizia AA Jr, Reiman HM, Myers RP, et al. Migration and granulomatous reaction after periurethral injection of polytef (Teflon). Jama. 1984;251(24):3277–81.
5. Chertin B, Puri P. Endoscopic management of vesicoureteral reflux: does it stand the test of time? Eur Urol. 2002;42(6):598–606. https://doi.org/10.1016/S0302-2838(02)00447-5.
6. Oswald J, Riccabona M, Lusuardi L, Bartsch G, Radmayr C. Prospective comparison and 1-year follow-up of a single endoscopic subureteral polydimethylsiloxane versus dextranomer/hyaluronic acid copolymer injection for treatment of vesicoureteral reflux in children. Urology. 2002;60(5):894–7. https://doi.org/10.1016/S0090-4295(02)01903-9.
7. Dean GE, Kirsch AJ, Packer MG, Scherz HC, Zaontz MR. Antegrade and retrograde endoscopic dextranomer/hyaluronic Acid bladder neck bulking for pediatric incontinence. J Urol. 2007;178(2):652–5. https://doi.org/10.1016/j.juro.2007.04.005.
8. Dyer L, Franco I, Firlit CF, Reda EF, Levitt SB, Palmer LS. Endoscopic injection of bulking agents in children with incontinence: dextranomer/hyaluronic acid copolymer versus polytetrafluoroethylene. J Urol. 2007;178(4 Pt 2):1628–31. https://doi.org/10.1016/j.juro.2007.05.092.
9. DaJusta D, Gargollo P, Snodgrass W. Dextranomer/hyaluronic acid bladder neck injection for persistent outlet incompetency after sling procedures in children with neurogenic urinary incontinence. J Pediatr Urol. 2013;9(3):278–82. https://doi.org/10.1016/j.jpurol.2012.03.013.
10. Pakkasjärvi N, Taskinen S. Does intraoperative success predict outcome in the treatment of urethral sphincter insufficiency with bulking agent? J Pediatr Urol. 2018;14(2):173.e1–173.e5. https://doi.org/10.1016/j.jpurol.2017.10.020.
11. Stout M, Alpert S, Ching C, et al. Outcomes after dextranomer/hyaluronic acid bladder neck injection in patients with urethral incontinence following bladder neck repair. J Pediatr Urol. 2023;19(6):743–8. https://doi.org/10.1016/j.jpurol.2023.07.002.
12. Alova I, Margaryan M, Verkarre V, Bernuy M, Lortat Jacob S, Lottmann HB. Outcome of continence procedures after failed endoscopic treatment with dextranomer-based implants (DEFLUX®). J Pediatr Urol. 2012;8(1):40–6. https://doi.org/10.1016/j.jpurol.2010.12.002.
13. Guys JM, Breaud J, Hery G, Camerlo A, Le Hors H, De Lagausie P. Endoscopic injection with polydimethylsiloxane for the treatment of pediatric urinary incontinence in the neurogenic bladder: long-term results. J Urol. 2006;175(3 Pt 1):1106–10. https://doi.org/10.1016/s0022-5347(05)00404-0.
14. Fiorenza V, Hukkinen M, Alova I, et al. Dextranomer endoscopic injections for the treatment of urinary incontinence in bladder exstrophy-epispadias complex. J Urol. 2023;209(3):591–9. https://doi.org/10.1097/ju.0000000000003086.
15. Shah BB, Massanyi EZ, Dicarlo H, et al. Role of urethral bulking agents in epispadias-exstrophy complex patients. J Pediatr Urol. 2014;10(1):176–80. https://doi.org/10.1016/j.jpurol.2013.08.004.
16. De Vocht TF, Chrzan R, Dik P, Klijn AJ, De Jong TP. Long-term results of bulking agent injection for persistent incontinence in cases of neurogenic bladder dysfunction. J Urol. 2010;183(2):719–23. https://doi.org/10.1016/j.juro.2009.10.044.
17. Kaye JD, Jafri SM, Cuda SP, Kalisvaart JF, Cerwinka WH, Kirsch AJ. Same setting laparoscopic antegrade continence enema and antegrade bladder neck injection for constipation and urinary incontinence in the spina bifida population. J Urol. 2010;184(4 Suppl):1644–50. https://doi.org/10.1016/j.juro.2010.04.018.
18. Riachy E, Defoor WR, Reddy PP, et al. Endoscopic treatment with dextranomer/hyaluronic acid for persistent incontinence after continent urinary reconstruction. J Endourol. 2015;29(2):137–40. https://doi.org/10.1089/end.2014.0326.
19. Eftekharzadeh S, Sabetkish N, Sabetkish S, Kajbafzadeh AM. Comparing the bulking effect of calcium hydroxyapatite and Deflux injection into the bladder neck for improvement of urinary incontinence in bladder exstrophy-epispadias complex. Int Urol Nephrol. 2017;49(2):183–9. https://doi.org/10.1007/s11255-016-1464-z.
20. Brosche T, Kuhn A, Lobodasch K, Sokol ER. Seven-year efficacy and safety outcomes of Bulkamid for the treatment of stress urinary incontinence. Neurourol Urodyn. 2021;40(1):502–8. https://doi.org/10.1002/nau.24589.
21. Sokol ER, Karram MM, Dmochowski R. Efficacy and safety of polyacrylamide hydrogel for the treatment of female stress incontinence: a randomized, prospective, multicenter North American study. J Urol. 2014;192(3):843–9. https://doi.org/10.1016/j.juro.2014.03.109.
22. Cerwinka WH, Scherz HC, Kirsch AJ. Dynamic hydrodistention classification of the ureter and the double hit method to correct vesicoureteral reflux. Arch Esp Urol. 2008;61(8):882–7. https://doi.org/10.4321/s0004-06142008000800005.
23. Läckgren G, Wåhlin N, Sköldenberg E, Nevéus T, Stenberg A. Endoscopic treatment of vesicoureteral reflux with dextranomer/hyaluronic acid copolymer is effective in either double ureters or a small kidney. J Urol. 2003;170(4 Pt 2):1551–5; discussion 1555. https://doi.org/10.1097/01.ju.0000084672.98131.f7.
24. Hunziker M, Mohanan N, Puri P. Dextranomer/hyaluronic acid endoscopic injection is effective in the treatment of intermediate and high grade vesicoureteral reflux in patients with complete duplex systems. J Urol. 2013;189(5):1876–81. https://doi.org/10.1016/j.juro.2012.11.048.
25. Cerwinka WH, Scherz HC, Kirsch AJ. Endoscopic treatment of vesicoureteral reflux associated with paraureteral diverticula in children. J Urol. 2007;178(4 Pt 1):1469–73. https://doi.org/10.1016/j.juro.2007.05.168.
26. Sheth KR, White JT, Stanasel I, et al. Comparing treatment modalities for transplant kidney vesicoureteral reflux in the pediatric

population. J Pediatr Urol. 2018;14(6):554.e1–554.e6. https://doi.org/10.1016/j.jpurol.2018.07.006.
27. Castagnetti M, Angelini L, Ghirardo G, et al. Ureteral complications after renal transplant in children: timing of presentation, and their open and endoscopic management. Pediatr Transplant. 2014;18(2):150–4. https://doi.org/10.1111/petr.12207.
28. Williams MA, Giel DW, Colleen Hastings M. Endoscopic Deflux injection for pediatric transplant reflux: a feasible alternative to open ureteral reimplant. J Pediatr Urol. 2008;4(5):341–4. https://doi.org/10.1016/j.jpurol.2008.04.003.
29. Vemulakonda VM, Koyle MA, Lendvay TS, et al. Endoscopic treatment of symptomatic refluxing renal transplant ureteroneocystostomies in children. Pediatr Transplant. 2010;14(2):212–5. https://doi.org/10.1111/j.1399-3046.2009.01196.x.
30. Cambareri G, Carpenter C, Stock J, Lewis J, Marietti S. Endoscopic antireflux surgery leading to obstruction in pediatric renal transplant patients. Pediatr Transplant. 2017;21(1). https://doi.org/10.1111/petr.12838.
31. Wu HY, Concepcion W, Grimm PC. When does vesicoureteral reflux in pediatric kidney transplant patients need treatment? Pediatr Transplant. 2018;22(8):e13299. https://doi.org/10.1111/petr.13299.
32. Mitrofanoff P. Trans-appendicular continent cystostomy in the management of the neurogenic bladder. Chir Pediatr. 1980;21(4):297–305.
33. Malone PS, Ransley PG, Kiely EM. Preliminary report: the antegrade continence enema. Lancet. 1990;336(8725):1217–8. https://doi.org/10.1016/0140-6736(90)92834-5.
34. Prieto JC, Perez-Brayfield M, Kirsch AJ, Koyle MA. The treatment of catheterizable stomal incontinence with endoscopic implantation of dextranomer/hyaluronic acid. J Urol. 2006;175(2):709–11. https://doi.org/10.1016/s0022-5347(05)00185-0.
35. Loufopoulos I, Konstantinos K, Pakzad M, et al. MP65–14 efficacy of polyacrylamide gel (Bulkamid®) injection in patients with mitrofanoff leakage after continent diversion surgery: a comparison with Macroplastique®. J Urol. 2023;209. https://doi.org/10.1097/JU.0000000000003323.14.
36. Kass-iliyya A, Rashid TG, Citron I, et al. Long-term efficacy of polydimethylsiloxane (Macroplastique) injection for Mitrofanoff leakage after continent urinary diversion surgery. BJU Int. 2015;115(3):461–5. https://doi.org/10.1111/bju.12817.
37. Koivusalo A, Pakarinen MP, Rintala RJ. Treatment of a leaking ACE conduit with Deflux injections. Pediatr Surg Int. 2006;22(12):1003–6. https://doi.org/10.1007/s00383-006-1792-7.