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REVIEW

Advancements in Surgical Management of Megaureters

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Abstract

Purpose of Review To review and describe the recent evolution of surgery for the various types of pediatric megaureter.

Recent Findings Megaureter management first relies on determining the underlying cause, whether by obstruction, reflux, or a combination, and then setting appropriate surgical indications because many cases do not require surgery as shown by observation studies. Endoscopic balloon dilation has been on the rise as a major treatment option for obstructive megaureter, while refluxing megaureters can also be treated by laparoscopic and robotic techniques, whether extravesically or transvesicoscopically. During ureteral reimplantation, tapering is sometimes necessary to address the enlarged ureter, but there are also considerations for not tapering or for tapering alternatives.

Summary Endoscopic and minimally invasive surgeries for megaureter have been the predominant focus of recent megaureter literature. These techniques still need collaborative prospective studies to better define which surgeries are best for patients needing megaureter interventions.

Keywords Megaureter · Vesicoureteral Reflux · Primary Obstructive Megaureter · Ureteral Balloon Dilation · Minimally Invasive Surgery · Robotic Surgery

Introduction

Megaureter is defined as an enlargement of the ureter, usually greater than 7 or 8 mm, and typically identified by ultrasound in pediatric patients [1–3]. Megaureter is an imaging finding only, and the underlying cause must be elucidated to determine appropriate management options, whether medical or surgical. The classic breakdown of etiologies is King's classification which is a two by two grid describing the presence or absence each of vesicoureteral reflux (VUR) and obstruction [4]. This classification gives the two main categories of primary obstructed (non-refluxing) megaureter (POM) and refluxing (non-obstructed) megaureter (dilating VUR), as well as the two less common groups of obstructed refluxing megaureter (ORM) and non-obstructive non-refluxing megaureter. Management in most scenarios is close observation without surgery; however, the decision for surgery as well as the surgical techniques have evolved over time. Each of these pathologies has unique aspects in management, but the general aspects of surgical management for a megaureter involve relieving obstruction or correcting reflux without introducing either in the post-surgical anatomy. Surgical principles are underscored by normal ureteral form and function, whereby antegrade flow of urine is permitted by an adequate ureteral diameter, allowing opposing wall coaptation for effective peristalsis [5]. Likewise, reflux is prevented by an adequate intramural submucosal tunnel to create an effective valve mechanism [6], combined with an appropriate ureteral orifice morphology [7, 8]. In treating pathologic versions of megaureter, the themes across pediatric urology of decreasing invasiveness by pursuing endoscopic and/or laparoscopic and robotic surgical options have likewise applied, as we have seen with endoscopic balloon dilation as well as laparoscopic and robotic versions of the highly successful traditional open ureteroneocystostomy (UNC) techniques.

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Determining Megaureter Type, and Indication for Surgery – Critical Underpinnings

Determining the specific megaureter type and defining the criteria for escalating to operative management are both critical for clinical practice, and likewise essential for appreciating the literature on the evolution of megaureter management. To this end, the typical evaluation of megaureter begins with a voiding cystourethrogram (VCUG) which, if showing no reflux, strongly suggests an obstructive process particularly in the presence of ultrasound findings of significant ureteral dilation, tortuosity, and/or intraluminal debris. Elucidating the presence of an obstructive element is the paramount priority, as obstruction (more so than reflux) has a higher morbidity rate and necessitates aspects of the surgical treatment (when necessary), such as requiring excision of the obstructive segment during reimplantation. The ultrasound and VCUG also provide evidence to rule out a secondary megaureter (such as from posterior urethral valves, neurogenic bladder, etc.), as confirming primary megaureter is critical as well before pursuing megaureter treatments. The typical next test to assess for obstruction is a diuretic renogram (DR) which can define split renal function and assess renal and ureteral washout for evidence of obstruction. Even when obstruction is confirmed, giving the diagnosis of POM, the recommended management is observation given that the majority of cases (around 72%) will improve and even resolve over time [9, 10]. When megaureter resolves, it occurs with gradual dilatation improvement from proximal to distal [11]. Factors associated with lower likelihood of resolution are higher grades of hydronephrosis and larger ureteral diameter [12], with one study reporting Society for Fetal Urology (SFU) hydronephrosis grades 3–4 and ureteral diameter > 13 mm as significant predictors for meeting surgical criteria [13]. A more recent prospective study of 50 ureters used a ureteral diameter of 10 mm as a cutoff, and found a 76% resolution rate over median 5 years for those less than 10 mm, and those ≥ 10 mm had a 17% resolution rate over a median of 9 years [14].

Surgical indications in POM studies most commonly cite the British Association of Pediatric Urologists 2014 consensus statement guidelines [3]. While these allude to clinical criteria such as urinary tract infections (UTI), pain, and nephrolithiasis, as well as progressive dilation on ultrasound, they focus their discussion on DR findings that should prompt surgery. Specifically, a delayed T ½ (greater than 20 min) or delayed washout curve is not enough to prompt surgery in an asymptomatic patient with stable or improving dilation. Rather, DR findings of an initial differential renal function (DRF) of < 40% or a drop in DRF by 5% or more on serial scans indicate surgery due to loss of function. Utilizing delayed washout as a surgical trigger is not recommended because in studies on both ureteropelvic junction obstruction and ureterovesical junction obstruction, kidneys with obstruction by delayed washout have continued to grow normally, maintain function, and even resolve their dilation. Likewise, washout curves in megaureter are particularly prone to inaccuracy at baseline, given that the region of interest outlined must include a dilated and often tortuous ureter, which may have various degrees of filling after diuretic administration and before draining [15, 16]. Given the limitations of renography in a megaureter, as well as the radiation exposure, cost, intravenous access, and bladder catheterization, some providers opt for no (or less frequent) renography and rather rely predominantly on serial ultrasound findings showing significantly increasing ureteral and pyelocaliceal dilation as an indication for surgery, in addition to clinical reasons above. These facts are particularly salient when considering the surgical outcomes literature, given that studies may utilize different surgical indication criteria as a limitation for comparing outcomes across studies.

The next section will continue with the focus on primary obstructive megaureter, given that moving on to clinical treatment of a refluxing megaureter can only be done if obstruction has first been ruled out. This brings up an important, and perhaps under-recognized, point about the existence of obstructed refluxing megaureter (ORM). Put simply, vesicoureteral reflux on a VCUG does not rule out obstruction. Findings on a VCUG that suggest an obstructive component in addition to reflux include the appearance of a normal or narrow caliber ureter at its distal 1–2 cm with significant ureterectasis proximal, as well as initial diluted contrast filling of a dilated ureter, or poor drainage of contrast from the ureter into the bladder on a late film [17]. Importantly, the main place in the literature where ORM is described is in cases of obstruction after endoscopic treatment of VUR with dextranomer/hyaluronic acid [18–20]. This fact should serve as a reminder to those considering treating cases of high-grade VUR with endoscopic injection, which has been done in significant volume in recent years [21], to first consider if an obstructive element could be at play.

The Evolution of Surgery for Primary Obstructive Megaureter

The historical gold standard for surgical treatment of POM has been ureteral reimplantation (UNC) with or without ureteral tapering. In infant cases, when reimplanting a dilated ureter into a small bladder can be a challenge (or, when needing immediate temporizing drainage in the

setting of active infection), a cutaneous ureterostomy is created with plans for subsequent UNC. Typically, tapering is not required if months of drainage via the ureterostomy has allowed for downsizing of the megaureter. Several additional strategies have developed in efforts to minimize the need for repeat open surgeries or tapering, while aiming to equal or improve the success seen with UNC. Ureteral stent placement is an option for internal drainage which can give more time for spontaneous resolution of megaureter, or can bridge infant patients until older to permit simpler reimplantation. Studies mostly from the 2000s reported that ureteral stents for POM were reasonably effective, in that about half of patients did not require subsequent surgery after 3 to 6 months of stenting. However, the fallbacks were that many infant POM ureteral stents required open placement, or had problems with UTI, stone formation, or migration [22–24]. More recently, a larger study (including 29 patients and 35 ureters) with longer follow-up (6 years) showed that 25% did not require subsequent surgery and there was a 40% rate of issues during the stenting period including UTI, hematuria, stones, and stent migration [25]. Other options arose which effectively sought to trade obstruction for reflux. These include an upfront dismembered refluxing reimplant, popularized by Kaefer, working as an internal temporary diversion rather than diverting to the skin via ureterostomy. In the report on 19 ureters managed this way, 18 went on to definitive surgery (as planned) after 1 year old: two had nephrectomy, and of the 16 undergoing reimplantation, 13 still required ureteral tapering [26, 27]. An evolution of this technique was proposed wherein a non-dismembered side-to-side refluxing reimplant is performed [28]. The group reporting this procedure proposed that the refluxing side-to-side technique could be considered the final management (with no follow-up surgery), particularly in circumcised males if there were no UTIs in the follow-up period.

Endoscopic balloon dilation (EBD) has gained popularity in the past 20 years for the treatment of POM, as it represents a completely endoscopic procedure that can typically eliminate the obstruction without introducing de novo VUR. For EBD, a high-pressure balloon is inflated under cystoscopic and fluoroscopic guidance to dilate the distal ureter and ureterovesical junction [29–47]. A cutting balloon or laser can also be employed in stenoses refractory to dilation alone [31, 37, 46, 48–50]. This procedure was first described in 1998 in Spain [29] with early small series from multiple centers up to the early 2010s. Most studies came out of Europe, predominantly Spain, Italy, and France except for a few series from other continents including only one from the United States (U.S.) [31], until recently [47]. Over the last decade, the number of studies and cases has risen significantly with later series involving larger numbers including 40 + [41, 45, 46] and even 100 + ureters [42].

Systematic reviews [51–54] of these series have borne out the primary advantage of EBD which is completely endoscopic treatment that is frequently a definitive management, not requiring subsequent ureteral reimplantation. Success rates, defined variably by lack of need for traditional surgery or improvement on imaging, range from 60 to 100% in the published studies. The theoretical downside of dilating the UVJ would be the introduction of VUR. However, Garcia-Aparicio et al. showed a 27% rate of postoperative VUR after dilating to 18 or 21 Fr by performing systematic VCUGs in follow-up [38]. Most study protocols only called for a postoperative VCUG in the setting of a febrile UTI during the follow-up period, and in this setting an approximately 8% rate of clinically significant VUR has been detected so far [53]. Challenges with EBD can be encountered with intubating the stenotic orifice or navigating stent placement into a tortuous ureteral system, but most studies describe technical feasibility on the first attempt and, rarely, repeat dilation or pre-stenting for a period can permit completion. Later studies have even described dilation without stent placement [45] and without fluoroscopy [42], but most describe fluoroscopic guidance and placement of a single stent. Although, the two U.S. studies in the literature describe the use of tandem stents [31, 47]. That there are only two U.S. studies on this topic in the literature to date would suggest low adoption so far in North America, but the rising description worldwide of EBD would suggest growing implementation related to advantages compared to the prior treatment options described above.

The primary caveat to EBD, as defined by a quality analysis from the European Association of Urology and European Society for Pediatric Urology (EAU/ESPU) systematic review [53], is that nearly all studies supporting EBD are retrospective single-center series, representing a relatively low level of evidence. This fact would suggest the need for a prospective study in the pediatric urology community, and perhaps one comparing key outcomes to the above-described alternatives would be a worthwhile next venture in the modern surgical management of primary obstructive megaureter.

Open Surgical Principles Applied Laparoscopically and Robotically

In some patients, surgical reconstruction is necessary (or preferred) over endoscopic treatment. The other clear trend in recent years has been to pursue the use of minimally invasive surgery (MIS) techniques to accomplish the equivalent of traditional open UNC. Generally, this has been done by either extravesical Lich-Gregoir reimplant laparoscopically, or intravesical reimplant varieties (Cohen cross-trigonal,

Glenn-Anderson advancement, etc.) which require a transvesicoscopic approach. A systematic review of studies comparing laparoscopic extravesical and transvesicoscopic techniques suggests that skilled operators achieve comparable success rates between the two approaches [55]. These (particularly transvesicoscopic), however, are performed by select surgeons at select centers given the challenges compared to open surgery: for example, the largest transvesicoscopic series from a single surgeon included 182 patients, 317 ureters, and all patients were selected to be 3 years or older with less than grade 5 VUR to prevent the need for tapering [56]. Most other transvesicoscopic series include significantly lower numbers [57–62]. Laparoscopic techniques like this have not had broad uptake related to technical challenges and concern by some that the advantages may be marginal compared to open surgery. Additionally, the cosmesis and recovery from a small Pfannenstiel incision may be difficult to improve upon, even with laparoscopy.

Robotic-assisted laparoscopic approaches overcome some of the technical challenges (of laparoscopic suturing, in particular) and as such have the potential for broader uptake in the setting of appropriate resources. While initial series on robotic ureteral reimplantation for primary VUR showed favorable outcomes [63, 64], there was a general hesitation when later series suggested lower efficacy and higher complication rates compared to open techniques [65–67]. More recently, series have shown improvement in robotic success rates [68, 69], perhaps illustrating the general learning curve associated with progress. Updated systematic reviews comparing open and robotic techniques for VUR have shown similar overall efficacy, possibly shorter hospital stay with the robotic approach (although this may be driven by practice pattern), but also typically longer robotic operative time [70–72]. The experience with laparoscopic and robotic reimplantation has grown to the point that the recently updated EAU/ESPU guideline on VUR acknowledges robotic and laparoscopic extravesical and transvesicoscopic techniques as reasonable options in terms of resolution and complication rates [73]. These studies, again, represent surgical treatments for primary VUR, which often does not involve a significantly dilated ureter.

When considering megaureter specifically, there have been some MIS studies focusing on the dilated ureter. A recent multi-institutional European study group on VUR compared open and robotic ureteral reimplantation in children with high grade (grades 4 and 5) VUR. Nine centers retrospectively reviewed 135 cases with mean age 11 months old and found a 94% clinical success in the open group and 98.5% clinical success in the robotic group. Notably, these were all cases that did not require tapering. The robotic group showed improved recovery parameters including shorter indwelling catheter time and shorter hospital stay [74]. Generally, many authors describe that the benefits of the robotic approach stand out in older patients or those with complex anatomy [75, 76].

Laparoscopic and robotic techniques for POM have also been described. Most studies employ an extravesical Lich-Gregoir technique after dismembering the obstructed ureter, with or without tapering. The largest series reported on 18 patients with a range of ages from six months to 15 years old who underwent robotic Lich-Gregoir. Of these, 39% underwent tapering intracorporeally, and all patients had improved hydronephrosis without the need for subsequent surgery over median two year follow-up [77]. Another series of studies described a laparoscopic (and subsequently robotic) extravesical cross-trigonal technique whereby the POM was reimplanted extravesically across the posterior bladder to increase tunnel length compared to that available for a standard Lich-Gregoir [78–80]. When 47 laparoscopic and 48 robotic cases by these techniques were compared across four centers, the result was similar success rates (94–97% over 8–12 month median follow-up) and low high-grade complication rates (2–4%) [81]. Transvesicoscopic techniques have likewise been applied for POM, but can be challenging. Li et al. compared laparoscopic transvesicoscopic Cohen reimplants to laparoscopic single-site Lich-Gregoir reimplants and found similar success and complication rates, but longer operative time and hospitalization for the transvesicoscopic technique [82]. One potential simplification for extravesical laparoscopic management of a dilated and tortuous megaureter can be extracorporeal tapering as illustrated by this study and others [82–86]. Another group employed a robotic technique for 16 infants wherein they extended the Lich-Gregoir to the anterior bladder wall in order to accomplish a longer tunnel. Of these, 25% required tapering and they reported a 94% success rate [85]. In comparing robotic to open POM reimplant outcomes, one single-center series from Italy included 11 robotic cases and 12 open cases and reported a similar OR time, shorter hospital stay for robotic cases, as well as similar success (91–92%) and complication (8–9%) rates [87].

Overall, select surgeons and centers are pursuing and publishing on laparoscopic and robotic surgeries for refluxing and obstructed megaureters. The literature to date in toto alludes to the fact that there are significant learning curves with limited broad update. Time to proficiency may be even further extended if endoscopic treatment rates via injection for VUR and balloon dilation for POM continue to rise as suggested by increasing reports in the literature. Furthermore, while transvesicoscopic techniques are depicted in the literature, they are rather infrequent due to the challenges and are likely to remain less common until smaller and more advanced robotic platforms, such as a miniaturized single-port platform, become available.

To Taper or Not to Taper

A unique aspect of megaureter reimplantation, more typically for an obstructive than a refluxing cause, is the potential need for ureteral tapering or tailoring. The pressure or impetus to taper in the modern era, however, is likely less pronounced than before for several reasons. First, the fundamental urological principle holds true that obstruction is worse than reflux. This fact is employed by the several surgical approaches for POM described above [26–28] which effectively trade obstruction for reflux as the lesser of two evils. Second, in the absence of infection, the field of pediatric urology has become gradually more permissive towards reflux in general. This has been evidenced by increasing observational management of VUR with decreasing surgical management over the past decades [88–90], not only waiting for reflux resolution but also observing in many instances as long as there are no significant clinical problems (i.e. febrile UTIs). Furthermore, many surgical outcome studies for POM and VUR no longer employ a planned VCUG during follow-up to define radiologic success, but rely solely on clinical success, wherein investigation with a VCUG is only pursued when prompted by a febrile UTI or other similar clinical problem. On the other side of the risk–benefit equation, UNC involving tapering has a higher operative complexity and higher complication rate, including urine leak, stricture, and VUR (whether by incompetent tunnel or ureterovesical fistula). Taking all these facts in the balance, the incentives in the current era point to a lower impetus to taper a megaureter when the necessity is in question.

For these reasons, ureteral tapering is likely done less frequently than in the past, although no study has borne out this suspicion. Important concepts associated with this logic, though, do appear in the literature that the surgeon should consider when undertaking megaureter surgery wherein the decision on tapering must be made. One concept is that a full 5:1 tunnel length to ureteral diameter ratio, as originally proposed by Paquin [6], may not be necessary [91]. This ratio in the megaureter can be challenging to achieve, especially in a small bladder. Permissiveness to a smaller ratio permits lesser (or no) tapering, a shorter tunnel, or both. Babu described what he called "mini reimplantation" of the megaureter wherein he employed no tapering during intravesical reimplant. He developed a 2:1 ratio tunnel in 13 patients wherein only two had postoperative reflux. This was a similar reflux outcome to 15 similar patients undergoing classic Cohen reimplants after excisional tapering, but the tapered cases had a higher rate of obstruction and higher overall need for reoperation [92]. Villanueva similarly presented a series of nine infants less than 6 months old requiring surgery for obstructive megaureter (4 ectopic, 5 POM). Instead of cutaneous ureterostomy, he performed a "mini" extravesical reimplant with a 2–3 cm tunnel regardless of ureteral diameter. He also performed "mini-tapering" in the last five patients wherein the distal 2–3 cm were tapered via the adventitia-sparing excisional technique described by Ossandon [93]. Two of the first four developed postoperative reflux, prompting his adaption to employ "mini-tapering" in the final cases, and none of the last five had clinically evident VUR over median follow-up of 44 months [94].

Further, it is not only the ratio of ureteral tunnel length to diameter that prevents reflux, but the configuration of the orifice may contribute to reflux prevention [7, 8]. Another valve mechanism addressing orifice configuration is the nipple valve [95–97]. This has recently been employed in the surgical management of POM, particularly in infant bladders that have limited domain for tunneling. Babu described laparoscopically securing the megaureter with 5 mm protruding into the bladder, combined with a short extravesical tunnel, as the treatment for 11 patients with POM ranging from five to 24 months old. He saw no VUR in this series on six month follow-up VCUGs [98]. Another group described a similar technique for POM, in which they employed no tapering and no tunnel, but instead secured the megaureter protruding into the bladder (with the distal end everted circumferentially) to achieve a ratio of intravesical length of nipple to ureteral diameter of about 2:1. In 13 cases, 11 were successful with one developing obstruction and one reflux. Several had cystoscopic follow-up and demonstrated persistence of a clear nipple-shaped orifice within the bladder [99]. In comparing tapered and non-tapered reimplants for POM, one series of 16 tapered ureters and 22 non-tapered ureters of similar initial diameter showed a higher rate of hydronephrosis resolution in the non-tapered group (50% vs. 19%), and each group needed one reoperation (one tapered for stricture, and one non-tapered for VUR) [100]. These studies illustrate the techniques and alternatives to tapering in the current era, which is more permissive of VUR than before.

The Path Forward and Conclusions

Surgical treatment of the megaureter continues to grow and evolve. Of paramount importance is determining the presence or absence of obstruction, and maintaining the understanding that even when reflux is present that there can be an obstructive component as well. Proving obstruction still depends largely on diuretic renography, which has its qualms, and so there are certainly opportunities for improvement in the testing and definition for the presence or absence of obstruction. Modifications of the Whitaker test [101] and

MR urography [102] have been attempted, but an ideal accurate and non-invasive test for ureteral obstruction still needs to be developed. Likewise, as has been alluded to above, the majority of the literature on surgical management of the megaureter comes from retrospective and single-center series. To further advance the field will require planning for prospective collaborative studies utilizing pre-defined surgical criteria and follow-up protocols. This will be particularly important for assessing newer technologies such as that seen employed increasingly with endoscopic balloon dilation for POM, as well as evaluations of future smaller and more sophisticated surgical tools and robotic platforms that are in development and will likely increasingly impact the field.

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

Compliance with Ethical Standards

Conflict of Interest The author does not have any existing conflict of interest.

Human and Animal Rights and Informed Consent All reported studies/experiments with human subjects performed by the author 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.

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