Spontaneous resolution and the role of endoscopic surgery in the treatment of primary obstructive megaureter: a review of the literature

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Abstract

The megaureter accounts for almost a quarter of all urinary tract dilations diagnosed in utero and is the second leading cause of hydronephrosis in newborns, following pyeloureteral junction obstruction. The current standard treatment for progressive or persistent, symptomatic primary obstructive megaureter is ureteral anti-reflux reimplantation, which can be associated with ureteral remodeling or plication. Due to the associated morbidity, postoperative recovery challenges, and the complications that may arise from the open surgical approach, there has been a natural inclination towards validating new minimally invasive techniques. This study reviews the literature, extracting data from three major international databases, from 1998 to 2022. Out of 1172 initially identified articles, only 52 were deemed eligible, analyzing 1764 patients and 1981 renal units. Results show that 65% of cases required surgical intervention, with minimally invasive techniques constituting 56% of these procedures. High-pressure endoscopic balloon dilation was the preferred endourologic technique. The degree of ureterohydronephrosis is considered one of the factors indicating the need for surgery. There is an inverse relationship between the diameter of the ureter and the likelihood of spontaneous resolution. Conditions such as renal hypoplasia, renal dysplasia, or ectopic ureteral insertion strongly indicate a poor prognosis. Endoscopic surgical techniques for treating primary obstructive megaureter can be definitive, first-line treatment options. In selected cases, they might be at least as effective and safe as the open approach, but with advantages like quicker recovery, fewer complications, shorter hospital stays, and reduced costs.

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Introduction

Congenital urological malformations are the first cause of chronic kidney failure in children, accounting for approximately a quarter of adult dialysis cases. In some instances, dysplastic changes in the renal parenchyma are present from birth. The progression towards atrophy and fibrosis is hastened when complications arise due to urinary stasis.[1]

As defined by the British Association of Paediatric Urologists (BAPU), a megaureter is characterized as a retrovesical ureter with a diameter exceeding 7 mm, after 30 weeks of gestation. This may or may not be accompanied by renal pelvis dilation. This definition is based on the radiological studies of Hellstrom.[2]

Smith, Stephens, and King have categorized megaureters into four types based on their etiology: refluxive, obstructive, refluxive-obstructive and non-refluxive/non-obstructive, which can be primary or secondary.[3]

Although the exact etiology of the primary obstructive megaureter remains unclear, the consensus leans towards the existence of an adynamic distal segment stemming from incomplete development. This segment may feature a patent obstruction and exhibit ultrastructural histopathologic changes - such as discontinuity of

smooth muscle fibers, abundant collagen deposits, and abnormalities in Cajal interstitial cells - which hinder peristalsis.[4]

While the ureteral meatus might appear normal and allow catheterism, it may prevent the spontaneous flow of urine, leading to a functional obstruction.[5] All these abnormalities compromise the intercellular junctions and disrupt the natural progression of peristaltic waves. Consequently, the physiological flow of urine is inhibited, causing functional obstruction and the dilation of the ureter.[6]

The current standard treatment for persistent or progressive symptomatic primary obstructive megaureter is ureteral anti-reflux reimplantation, typically associated with ureteral remodeling or plication. Short-term alternatives encompass procedures like double-J stenting, endoscopic balloon dilation, endoureterotomy, cutaneous ureterostomy, and refluxing ureteral reimplantation. Surgical intervention is commonly indicated in 10-25% of cases, usually by the age of 7, particularly when renal function drops below 35-40% or in the presence of advancing ureterohydronephrosis, recurrent urinary tract infections, bilateral disease, or a solitary kidney.[2,3,5]

The traditional approach to accessing the ureter can be intravesical (*e.g.*, Cohen, Glenn-Anderson), extravesical (*e.g.*, Lich Gregoir), or a combination of the two (*e.g.*, Politano-Leadbetter). The affected ureter is usually redundant and tortuous. Its capability to transport urine by peristalsis diminishes as its diameter increases. Therefore, procedures such as plication or excision, which aim to gradually reduce the ureter's size, are often necessitated. When performing these procedures, preserving vascularity is paramount.[7]

Excision remodeling is typically favored in cases of extreme dilations, or patients with small-capacity bladders. Otherwise, plication is performed.[8] Plication brings benefits like preserving vascularization and reducing risks of fistulas or stenosis. However, in conditions of significant dilation, the reimplantation process is more technically challenging. Success rates reported for plication range between 93-95%, while for excision remodeling, it varies between 74-90% (Figure 1).[7,9,10]

Materials and Methods

We initiated a systematic search of the literature to evaluate the indications, efficacy, and complications of currently available treatment options for primary obstructive megaureters, thoroughly focusing on endoscopic procedures.

Three of the main international databases of specialized publications, Pubmed, Science Direct, and Scopus, were systematically searched on December 1, 2022. Articles discussing the definition, pathophysiology, diagnostic modalities, prenatal and postnatal investigations, as well as the therapeutic approach and surgical options currently available for primary obstructive megaureter were identified and analyzed. Mendeley Reference Management Software was used to remove duplicates.

The search terms used were "obstructive megaureter", "obstructive megaloureter", "obstructive hydroureter", "primary megaureter", "ureterohydronephrosis", and "non-refluxing megaureter". We selected only full-text articles published in English between 1998 and 2022, that involved pediatric patients. Case presentations were excluded. The systematic search targeted articles published since 1998, the year when Angulo first reported high-pressure endoscopic balloon dilation of the vesicoureteral junction obstruction, as a new temporary treatment for primary obstructive megaureter.[11]

Two independent reviewers (a specialist and resident pediatric surgeons) evaluated abstracts and full-text articles of interest, extracting data regarding the age at diagnosis, sex of the patient, antenatal diagnosis, radiologic and functional findings, age at surgery, serum urea and creatinine levels, history of urinary tract infections, glomerular filtration rate, type of intervention, need for ureteral stents, hospital stay, prophylactic antibiotic therapy, incidents, complications, readmissions rate, patient satisfaction, histopathological findings, and secondary procedures. These were centralized in a Microsoft Excel data sheet.

Patients who had undergone previous operations or had associated pathologies such as vesicoureteral reflux, ureterocele, urinary tract duplication, posterior urethral valves, or neurogenic bladders were excluded from the study.

Results

Of the 1,172 articles identified, 226 full-text articles were selected (Figure 2). After removing duplicates, case presentations, and studies involving adults or animal models, 52 articles (46 retrospective and 6 prospective) were deemed eligible for the study. In total, 1,769 patients and 1,976 renal units were analyzed.

Surgery was necessary in 65% of cases, with 56% of all opera-

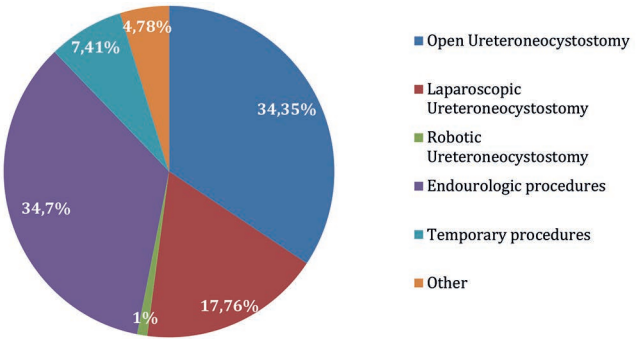

Figure 1. Surgical procedures.

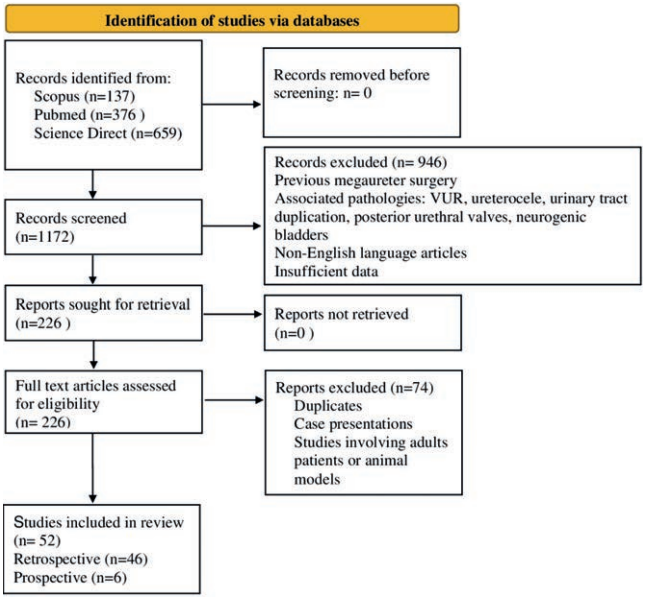

Figure 2. Prisma Flow Diagram. Redacted according to BMJ 2021;372:n71.

tions being minimally invasive procedures. Of all the endourologic procedures, which made up 34% of the total, high-pressure endoscopic balloon dilation was the first-line treatment in 73% of cases (representing 24% of all procedures).

Ureteroneocistostomy was the most frequently adopted therapeutic solution, used in 73% of cases. Of these, 35% were realized by a minimally invasive approach.

The most widely accepted diagnostic criteria aligned with the BAPU definition was a distal ureter wider than 7 mm in diameter.

Postnatal investigations for babies diagnosed with hydroureteronephrosis usually begin with an ultrasound scan. This scan evaluated the diameter of the pelvis, the echogenicity of the parenchyma, and the route, dimensions, and insertion of the ureter. Typically, the first ultrasound was conducted after 48 hours of life, except in emergency cases.

This initial scan was usually followed by a voiding cystourethrogram (VCUG) or an echo-enhanced ultrasound voiding cystography to visualize the bladder wall and rule out conditions like a posterior urethral valve, ureterocele, or vesicoureteral reflux. Subsequently, a diuretic renogram was performed to confirm any obstruction and gauge its impact on renal function, which would help determine the need for surgery.

Primary surgical indications included progressive dilatation with parenchyma thinning, renal function impairment (DRF < 40%), an obstructive pattern on the excretory phase of a diuretic isotopic renogram, and recurrent febrile UTI in the absence of vesicoureteral reflux or posterior urethral valves. Scintigraphy was considered suggestive of obstruction if T ½ of the radionuclide exceeded 20 minutes post-diuretic injection.

The degree of hydroureteronephrosis is considered one of the predictive factors in determining the need for surgery. There exists an inverse relationship between the diameter of the ureter and the likelihood of spontaneous resolution.

Discussions

Even though diagnosis has become easier, deciding the optimal treatment remains challenging. Many cases might be treated conservatively, as the distal ureter might continue to mature after birth.

The presence of renal hypoplasia or dysplasia on initial ultrasound strongly predicts poor outcomes. After a 7-year follow-up, spontaneous resolution rates were between 60-70%. No patients with ureters wider than 15 mm experienced spontaneous regression.[12]

Ureteral dilation is more severe in ectopic megaureters, and renal function deteriorates despite early surgery, compared to orthotopic megaureters. Cases with ectopic insertions, often associated with renal dysplasia, do not resolve spontaneously.[13]

In a 2016 study on 25 patients under 12 months, Drlik found no significant differences in outcomes between two groups with differential renal function of 10-40%, whether treated conservatively or surgically. Early surgery indications in asymptomatic and radiologically stable patients should not solely rely on an initially low DRF.[14,15]

The time required for spontaneous resolution increases with the severity of antenatally detected hydronephrosis. Factors such as time of presentation, hydronephrosis degree, and distal ureter dilation influence spontaneous resolution rates, which can be up to 71% for grades I-III and 55% for grade IV, at 3 years old.[16]

Ureter sizes below 11 mm are strongly associated with spontaneous resolution, while diameters over 14 mm predict the necessity for surgery.[17] These values are also supported by Manzoni, who considers that in cases where the pelvic diameter exceeds 15 mm and the calyces are dilated, the surgery is very probable.[18]

The median age for resolution in patients with a cross-sectional diameter of 6-10 mm was 14.5 months, while for diameters from 11 to 15 mm was 43 months, in a long-term follow-up study published by Arena in 2012.[19]

Criteria such as differential renal function below 30%, ureteral diameters over 13-15 mm, and higher hydronephrosis grades are surgical predictors, as considered by Chertin in a long-term follow-up study published in 2008.[20]

In an article published in 1998 in "Cirugía Pediátrica", the journal of the Spanish Society of Pediatric Surgery, Angulo presented the experience of the clinic from the Hospital Universitario Puerta del Mar in Cádiz, being the first author to describe endoscopic balloon dilation of the ureterovesical junction, followed by a double J stent insertion, in a child.[11]

High-pressure balloon dilation of the ureterovesical junction has comparable success (86% *vs* 91%) and reintervention rates as open reimplantation.[21] It is a minimally invasive, safe, and feasible technique for treating primary obstructive megaureter, even under 1 year of age.[22] If the result of endoscopic dilation is satisfactory at 18 months postoperatively, in most cases, it will be maintained over time.[23]

The success of dilation relates to the ureteral orifice appearance. Long stenosis (over 2-3 cm) or the identification of a ureterocele-like orifice at cystoscopy is associated with a poor outcome. This procedure may be the first therapeutic approach for children of all ages, preserving ureteral vascularization.[24]

High-pressure endoscopic balloon dilation may be a definitive treatment for primary obstructive megaureter in infants, with a nearly 90% success rate in selected cases, as shown by multiple multicentric studies.[25-28]

Patients with short stenotic tract (under 5-10 mm) are best candidates for endoscopic dilation if the ureteral ostium is not placed in a bladder diverticulum.[29]

The general opinion regarding possible causes of primary obstructive megaureter is focused on ultrastructural changes in muscle cells, generating an aperistaltic distal ureteric segment. Despite this, in many cases (approx 80%), a real stenotic ring causing obstruction was observed during endoscopic dilation.[22,30]

In those cases where the stenotic ring is still visible after endoscopic dilation, a cutting balloon ureterotomy may be performed, with an overall success rate of 83%.[31] Endoureterotomy has a high success rate, even for patients under 1 year of age, avoiding complications associated with open surgery.[32]

A ureter with a diameter of more than 15-25 mm is one of the contraindications for endoscopic balloon dilation. In these cases, the authors found, according to existing information in the literature, that ureterovesical reimplantation with ureteral remodeling provides superior results on peristaltic improvement and postoperative evolution.[33]

Regarding the most common postoperative complications, were analized the incidence, predisposing factors, and therapeutic approach for vesicoureteral reflux diagnosed after endoscopic balloon dilation of the ureterovesical junction.

The presence of diverticula adjacent to the ureteral meatus is a factor considered predisposing to the occurrence of postoperative vesicoureteral reflux. Its exact incidence is unknown because most authors recommend urinary cystography only in the presence of recurrent urinary tract infections. It has been found that recurrence of dilatations in restenosis cases is not associated with an increased risk of developing postoperative VUR.[34]

The confirmation of obstruction on renogram is considered a significant predictor of UTI, whose rate is negligible for patients with mild dilatation. An incidence of 20% for symptomatic UTIs may be observed in patients with moderate or severe dilatation, even

under continuous antibiotic prophylaxis. The incidence of UTI is higher in the first year of life but decreases with antibiotic prophylaxis, reducing by 55% after the first year.[12,35]

Continuous antibiotic prophylaxis and circumcision decrease febrile urinary tract infection rates. To prevent one febrile UTI, it is necessary to prescribe continuous antibiotic prophylaxis to three children and to perform circumcision in five boys.[36]

Regarding primary stenting as a definitive treatment for POM in children, this approach has a success rate of 26% in long-term follow-up and may be used as a temporary procedure for children under 1 year of age. This procedure was not successful if the distal ureteral diameter measured over 12 mm after stent removal. However, no criteria suggesting in which patients this procedure would be successful could not be established. Stent-related complications were related in 41% of cases. A controversial issue is the need and duration of stent maintenance. Mounting a double J stent at the level of a tortuous ureter is a laborious, time-consuming process that involves irradiation, repeated anesthesia, and possibly further complications.[37,38]

Double stenting comes with high morbidity and technical challenges but can be a temporary measure in compromised renal function cases.[39,40]

Conclusions

Prenatal ultrasound scans have changed the perspective on the diagnosis, treatment, and follow-up of various uropathies, allowing for detection even before symptoms manifest.

With advancements in prenatal and postnatal diagnostic modalities, the detection rate has improved, but the optimal treatment pathway remains debatable.

The duration required for spontaneous resolution extends as the severity of antenatally detected hydronephrosis increases. The presence of renal hypoplasia, renal dysplasia, or an ectopic ureteral insertion serves as a strong indicator of unfavorable outcomes in the absence of surgery.

The trend in managing primary obstructive megaureters has evolved over the years, transitioning from traditional open surgical procedures towards minimally invasive techniques. Surgical techniques using endoscopic approaches in treating primary obstructive megaureter may be definitive, first-line therapeutic methods. These are not only as effective and safe as the open approach but also associated with a quicker recovery, fewer complications rate and reduced hospitalization costs.

High-pressure endoscopic balloon dilation stands out as a minimally invasive technique, offering high success rates, shorter hospital stays, and fewer complications, making it suitable even for children under 1 year of age, in selected cases. However, specific anatomical and pathological considerations, such as ureteral stenosis length and orifice characteristics, impact its success rate.

In conclusion, despite diagnostic advances, treatment decision-making for primary obstructive megaureters remains complex, necessitating a nuanced approach based on multiple clinical factors.

This comprehensive review, encompassing two decades of literature, underscores the dynamic nature of primary obstructive megaureter management. While endoscopic approaches offer promising outcomes, patient selection remains crucial. As the field continues to evolve, more long-term studies and randomized controlled trials are required to establish definitive guidelines for the optimal management of these patients.

The decision-making process for optimal treatment modalities remains intricate, necessitating a judicious evaluation of spontaneous resolution probabilities and predictive surgical indications based on the severity of the condition and associated renal functional implications.

Variability in study designs and outcome measures limited the ability to perform meta-analyses. Publication bias may influence the review, as negative or inconclusive results may be underrepresented in the literature. The studies included in this research were of moderate quality and non-randomized. Nevertheless, the sample sizes were representative, and the follow-up periods were generally adequate, resulting in relevant outcomes in most cases.

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