

News on pediatric urology

Giuseppe Masnata, Valeria Manca, Laura Chia, Francesca Esu

Pediatric Urology and Urodynamics, "G. Brotzu" Hospital, Cagliari, Italy

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From the womb to the adult

Guest Editors: Vassilios Fanos (Cagliari, Italy), Michele Mussap (Genoa, Italy), Antonio Del Vecchio (Bari, Italy), Bo Sun (Shanghai, China), Dorret I. Boomsma (Amsterdam, the Netherlands), Gavino Faa (Cagliari, Italy), Antonio Giordano (Philadelphia, USA)

Abstract

Pediatric urology is a pediatric speciality dedicated to the diagnosis and treatment of congenital and acquired genitourinary tract diseases. It is a speciality that is rapidly changing, thanks to the technological development that has been emerging in recent years. There have been important diagnostic and therapeutic news.

Congenital anomalies of the kidneys and urinary tract (CAKUT) include various entities of structural malformations that result from defects in their morphogenesis. Clinical research and genetic studies on the origins of CAKUT are quickly evolving, with significant growth of high-quality research.

Management goals of CAKUT include prevention of febrile urinary tract infections (UTIs) in newborns and toddlers and renal injury, while minimizing the morbidity of treatment and follow-up. Treatment options include observation with or without continuous antibiotic prophylaxis (CAP) and surgical correction. Now, randomized controlled studies show that children with normal urinary tracts or low-grade vesicoureteral reflux (VUR) do not benefit from prophylaxis.

All children with known mechanical or functional obstructions of the urinary tract are considered to have UTI. Functional obstruction often results from lower urinary tract dysfunction (LUTD) of either neurogenic or non-neurogenic origin and dilating VUR.

The role of bladder and bowel dysfunction (BBD) in children with UTI and the long-term risk of renal scarring have shed new light on treatment strategies. Often it is BBD, rather than reflux, that causes UTI in children older than 2 years.

Pediatric urology has evolved in recent years, with a greater focus on bladder and renal function, minimally invasive treatment, evidence-based interventions, and guideline adherence.

Other topics in pediatric urology include urinary incontinence in children with special needs and the use of robot-assisted laparoscopic surgery (RALS) in children, with advantages over conventional laparoscopic surgery.

Keywords

CAKUT (congenital anomalies of the kidneys and urinary tract), CAP (continuous antibiotic prophylaxis), UTIs (urinary tract infections), LUTD (lower urinary tract dysfunction), BBD (bowel bladder dysfunction), RALS (robot-assisted laparoscopic surgery).

Corresponding author

Giuseppe Masnata, Urologia e Urodinamica Pediatrica, Azienda Ospedale "G. Brotzu", Cagliari, Italy; email: giuseppemasnata@gmail.com.

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Congenital anomalies of the kidneys and urinary tract

Congenital anomalies of the kidney and urinary tract (CAKUT) present with varying degrees of severity, are often part of a genetic syndrome or may be associated with morphological changes in other parts of the body. More than 500 syndromes have been described, characterized by combined defects of the kidney and other organ systems [1].

CAKUT accounts for up to 40% of pediatric end stage renal disease (ESRD) and a significant proportion of adult nephropathy. CAKUT includes a wide range of structural and functional malformations of the renal system, that occur in the kidney (e.g., hypoplasia and dysplasia), collecting system (e.g., hydronephrosis and megaureter), bladder (e.g., ureterocele and vesicoureteral reflux [VUR]), or urethra (e.g., posterior urethral valves) [2].

CAKUT is relatively common, affecting up to 2% of pregnancies. Therefore it is important the multidisciplinary approach for their accurate diagnosis and therapy [3]. The prevention of kidney

damage is achieved with a proper application of modern guidelines, which, in most cases, provide a conservative approach, not surgery.

Recently, the British Association of Paediatric Urologists has recommended, for newborns with prenatally diagnosed hydronephrosis, antibiotic prophylaxis and investigation with an ultrasound scan and micturating cystourethrogram, followed by a diuretic renogram once VUR and bladder outlet obstruction had been excluded [4].

In our opinion it is important to detect the possible presence of a visible ureter during fetal life and then confirm its presence with ultrasound, a week after birth.

In any case, we need less invasive techniques for diagnosis of VUR and better understanding of the contribution of VUR and other risk factors to the development of renal function abnormalities [5].

Many authors proposed guidelines for the management of the antenatal pelvic dilatation at birth with variable cut-off of posterior anterior diameter. These guidelines are important to identify neonates who need an imaging evaluation to avoid subsequent infections and renal scars.

But, despite the efforts of clinicians, no universal guidelines for the clinical management of patients with mild to moderate antenatal hydronephrosis (ANH) are currently available.

Conservative management of patients with CAKUT is often recommended, with surgery reserved for patients with clinical symptoms or declining renal function. Management options include observation with or without continuous antibiotic prophylaxis (CAP) and surgical correction via endoscopic, open or laparoscopic/robotic approaches [6]. Anyway, surgery is rarely performed on children with CAKUT younger than 1 year of age, except in cases of recurrent febrile UTIs. With early and multidisciplinary management of these neonates and children, we already noticed a delay in renal function progression, however there is a strong need to identify predictive factors to improve long-term prognosis. Even for this, there is an immense need for transitional care of patients with CAKUT as they grow into adulthood [7].

Finally, collaborative efforts are needed to collect large cohorts of patients with CAKUT and to integrate the data from epidemiologic, clinical, genomic, epigenomic, transcriptomic, and proteomic studies [8]. Advances in pediatric urology appear quick and interesting, accompanied by great attention by neonatologists and pediatricians.

Urinary tract infections and continuous antibiotic prophylaxis

Urinary tract infections (UTIs) represent the most common bacterial infection in children. UTI affects about 2 % of boys and 8% of girls during the first 6 years of life with *E. coli* as the predominant pathogen. UTI causes discomfort and concern and VUR may be associated with damage of renal parenchyma, congenital or acquired, known as reflux nephropathy, which may be responsible for the development of chronic renal failure in adults. Neonatal UTI is frequently complicated by bacteraemia.

The strong correlation between febrile UTI, dilating VUR and renal scarring, led to the introduction of CAP for children at risk.

In the past, the investigation and management of UTIs in young children has been aggressive, with renal imaging and VCUGs universally recommended for the detection of VUR.

It has become a common practice to use prophylaxis for children with VUR and other CAKUT [9].

High-grade prenatal hydronephrosis is also a significant risk factor for febrile UTIs in newborn and infant, with significantly higher febrile urinary tract infection rates. Therefore, those patients may benefit from CAP.

The efficacy and the effectiveness of CAP in children with congenital ANH and in patients with VUR, is doubtful and then this policy has been questioned because of a lack of scientific support. The literature has both supportive and contradictory evidence, and now randomized controlled trials are available comparing prophylaxis with no treatment or placebo.

The RIVUR study [10] and the PRIVENT trial [11] have demonstrated that treating recurrent UTIs with CAP, indeed, can prevent the recurrence of UTIs. In at least one Cochrane review [12], it was also reported that there is no current evidence that surgical correction prevents important outcomes such as scarring. Recent studies and guidelines suggest that CAP has little or no role in preventing UTI in children with low grades (I and II) of VUR and in newborns without a high grade of ANH and visible dilated ureters. After the first year of life, children have very few relapses of UTI and don't need CAP, except in the case of complicated double district with VUR. However, in selected patients CAP is able to protect against recurrent UTI and long-term sequelae [14]. Moreover, CAP

presents a risk of breakthrough infections, adverse drug reactions and also it is associated with the risk of developing antibiotic resistance.

Thus, in recent times, there was a decrease in the use of CAP because of the questioning of its effectiveness, increasing bacterial resistance, and low adherence to therapy.

So alternative measures to reduce UTI recurrence should be recommended. Cranberry is also effective in reducing the number of recurrences and related antimicrobial used in children [15]. Deliberate colonization of the human urinary tract of patients with recurrent UTI with *E. coli* 83972 has resulted in subjective benefit. The non-pathogenic *E. coli* isolate NU14 Delta waaL is a candidate to develop live-attenuated vaccine for the treatment and prevention of acute and recurrent UTI. In children toilet-trained, diagnosing and treating dysfunctional elimination syndromes decrease the incidence of recurrent UTI. A recent meta-analysis did not support routine circumcision for normal boys with no risk factors [16].

VUR management has been for many years and is still controversial. In contrast to recently published studies and guidelines, different meta-analysis supports CAP in children with VUR [17]. More studies are needed to support this finding and it's necessary to establish the relationship between UTI in infants and young children and reduced renal function and hypertension in adults [5].

Large-scale prospective studies have questioned the benefits of CAP and surgical intervention, except in patients with high-grade dilating VUR.

VUR is not a homogeneous condition affecting homogeneous patients and management should be individualized and based on patient age, health, risk of subsequent renal injury, clinical course, renal function, and parental preference [18].

Lower urinary tract dysfunctions and bowel bladder dysfunction

Children with lower urinary tract dysfunctions (LUTD) are widely represented in a school age population (15-20%). More than 50% of children with LUTD are affected with functional constipation (bowel and bladder dysfunction, BBD). Undiagnosed constipation plays a role in the higher incidence of dysfunctional voiding in children training late [19].

In 2010, the American Urological Association (AUA) reported that BBD, which is common in patients with VUR, increases the risk of breakthrough

UTI in children receiving CAP, reduces the success rate for endoscopic injection therapy, and increases the risk of postoperative UTI, irrespective of the surgical success rate for VUR [20].

VUR and BBD are risk factors for recurrent UTI in children, especially when they appear in combination, with high risk of renal scarring.

According to ICCS, investigation of BBD needs non invasive integrated urodynamic studies, compilation of frequency/volume chart and gastroenterologic approach with Bristol stool form scale, completed from uroflowmetry with electromyography, ultrasound study of bladder with maximum cystometric capacity, post-void residual urine volume and rectal diameter. The non invasive urodynamic integrated approach is inexpensive, sensitive, well accepted and could better explain in future the aetiology and physiopathology of BBD [21]. The existence of a common neuromuscular disorder should be the base for both bladder and bowel dysfunction [22].

Successful treatment of BBD is based on bladder retraining associated to constipation therapy. Some children have refractory constipation, some others respond well to treatment, but once treatment is discontinued most children relapse back into their constipation. In the solved cases, it also has a subsequent disappearance of recurrent UTI.

Robot-assisted laparoscopic surgery

Minimally invasive or laparoscopic surgery uses small incisions and telescopes to perform surgeries that previously had been performed with larger incisions. Studies have shown that minimally invasive pyeloplasty techniques are safe, effective and feasible in adult and pediatric populations [23].

Robot-assisted laparoscopic surgery (RALS) is also minimally invasive surgery but uses a surgical robot that allows surgeons to perform more complex surgeries. RALS procedures are evolving. Data from the literature and clinical results are encouraging. RALS has been proven to be safe and effective for various urological procedures in children, with outcomes comparable to open procedures and it has several advantages over conventional laparoscopic surgery [24].

The procedure most performed with the da Vinci® Surgical System in pediatric urology is pyeloplasty for ureteropelvic junction obstruction. Other procedures can be performed with the robot, such as duplex kidney heminephrectomy

and ureteroureterostomy, pyelolithotomy, ureteral reimplantation, bladder neck reconstruction, augmentation cystoplasty and appendicovesicostomy.

The robot system allows delicate and precise movements, which are ideal for reconstructive surgeries that children with urological issues often require. RALS has been shown to be a safe and effective treatment in children with comparably low complications rates. It has benefits like its safety profile and reduction in mean postoperative hospital stay, compared with conventional procedures. Also reduction of the morbidity associated with open surgery and facilitation of a more rapid recovery. In addition, both patients and parents prefer the smaller surgical scars associated with RALS to those resulting from open surgery. However, it is typically associated with longer surgical time and material cost.

Further, large randomised studies are required to compare the operating times and outcomes in comparison to the laparoscopic approach [25].

Declaration of interest

The Authors declare that there is no conflict of interest.

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