Various aspects of transition of care for adolescents with urological conditions

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Abstract

Transition into adulthood is a common issue in many disciplines. However, urology faces additional difficulties due to different models of care and training as well as a wide diversity of pathologies. The goal of this paper is to discuss various aspects of the transition of urological care.

This review provides some examples of pathologies that might require special attention of specialists. Most patients with rare diseases must be closely followed up in the long term. However, high-volume conditions may also have a huge impact on the well-being and quality of life in adulthood. Children who are cured due to oncological conditions will probably need additional attention in adulthood. The urological care during childhood is provided by a pediatric urologist, a pediatric surgeon or a urologist, depending on the local regulations and the organization of care. All patients are subsequently referred to a general urologist. Nowadays, a multidisciplinary approach is recommended in many cases, with a pediatric urologist as one of the team members.

The patient, caregivers and healthcare professionals must be fully involved and focused on close cooperation to make the transition process smooth and successful.

Key words: transition, urology, congenital genitourinary conditions

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Introduction

Transition into adulthood is a common issue in many disciplines. Urology may face additional difficulties due to possessing different models of care and professional training as well as to a wide diversity of pathologies.

More and more children with severe congenital and acquired diseases of the urogenital system enter adulthood as medicine is developing. Congenital anomalies of the kidney and urinary tract (CAKUT) are the common cause of end-stage renal disease (ESRD) in the pediatric population. Maintaining good renal function is the main goal in patients with CAKUT. Proper care from the neonatal period has a huge impact on the survival rate and the quality of life in patients with serious congenital anomalies.[1,2] For the most severe cases, delaying the necessity of renal replacement therapy (RRT) is also of great importance. Nowadays, kidney transplantation can be applied in children who have had major urological interventions, and the survival rate at 10 years is similar as in the case of kidney transplantation performed at presence of the native and healthy bladder.[3] There is also no significant difference in mortality after transplantation in patients with spina bifida.[4] However, many patients with stable chronic kidney disease (CKD) during childhood progress to ESRD requiring RRT during adulthood. The median age at the start of RRT is significantly lower in the CAKUT cohort (31 years) than in the non-CAKUT cohort (61 years).[5]

Due to well-organized care, newborns can survive the most critical period and proper management can be provided through childhood. Puberty is a critical moment for the adolescents who need a long-term follow-up, as some are less cooperative. During this period of life, these adolescents should also be trained on how to take care of themselves to make the transition into adulthood as smooth as possible, minimizing the risk of failure, and to ensure a good quality of life. Therefore, improving management during transition to postpone the need for RRT should be the goal of the healthcare providers in the future.

Objectives

The aim of this paper was to discuss various aspects of the transition of urological care as well as provide examples of pathologies that might require special attention of healthcare professionals.

Methodology

A PubMed search was performed in October 2020. Articles published in English between 2000 and 2020, and related to the transition of patients with selected urological conditions (key words: 'neuropathic bladder'; 'posterior urethral valve'; 'exstrophy-epispadias complex'; 'disorders of sexual development'; 'anorectal malformations'; 'hypospadias'; 'urinary incontinence'; and 'pediatric oncology') were selected. Most of the articles were reviews and expert opinions. The authors assessed the content of the abstracts, and then the articles were subjected to further evaluation. Finally, 43 articles were approved by all authors to discuss the epidemiology, clinical course, prognostic factors, and long-term follow-up of the selected conditions. There are hardly any original studies focusing on this topic, which obviously might have influenced the selection process.

Transition into adulthood

Long-term follow-up: By whom?

Pediatric urology is a subspecialty of both urology and pediatric surgery, depending on the local regulations. This may impact the transition of care. Professionals with a pediatric surgical background are familiar with a wide range of different congenital anomalies involving other organs/systems, such as anorectal malformations (ARMs). Those with urology as a background are better prepared to deal with the common problems in adulthood, such as tumors. Szymanski et al. stated that urologists could provide the best care for patients who require a long-term follow-up.[6] According to Hsieh et al., the knowledge of congenital genitourinary conditions (CGCs) among general urologists is limited and they need additional training.[7] There is no literature on this topic referring to pediatric surgeons who deal with CGCs. They are, however, mostly involved in the transition of patients with congenital diseases of the gastrointestinal tract (e.g., Hirschsprung disease, ARMs).[8]

There is a recent tendency for the centralization of care in order to improve its quality. High-volume centers are thought to be the best solution to achieve good outcomes with acceptable complication rates. At the same time, proper medical training for healthcare professionals must be maintained. In some countries, children with rare urological diseases (e.g., exstrophy-epispadias complex (EEC), disorders of sexual development (DSD), tumors) are treated only in a limited number of dedicated units. An important implication of this model is a limited exposure of the trainees to the whole spectrum of pediatric urological cases outside those centers. The centralization of cases in one place means less experience in other locations. In terms of transition of care, this can have an adverse effect on a proper follow-up, as only few professionals can acquire adequate knowledge in this field.

Many patients with rare anomalies require a multidisciplinary approach during childhood. Depending on the condition, a pediatric urologist is part of the team, together with an endocrinologist, a nephrologist, a neurosurgeon,

a pediatrician, and a psychologist. Before entering adulthood, a clear summary of the medical history must be provided to the patient. Nevertheless, the question arises as to who should follow up the adult patient 20 years after feminizing surgery – a gynecologist or a urologist? Is a multidisciplinary approach required, and if so, who should be in charge – an endocrinologist or a gynecologist? What if the patient is not fully prepared mentally to take care of themselves?

Long-term follow-up: For whom?

There is no doubt that some individuals with congenital anomalies or acquired conditions will need a long-term follow-up. These individuals may present with rare and common diseases. Some may be at risk of impairment during their lifetime, but for some, the clinical course is not really known. Taking all the above into consideration, several different groups of patients can be defined.

Low-volume and rare anomalies with long-term consequences

Neuropathic bladder

Neurogenic lower urinary tract dysfunction (NLUTD) in patients with spinal dysraphism is the most frequently described model of transition in pediatric urology. Spina bifida is a common neurologic abnormality, with worldwide incidence estimated at 0.3–4.5 per 1000 births. The main goal of the urological management is to protect the upper urinary tract (UUT) and maintain good renal function by means of a proper control of the bladder function. Another important factor for obtaining optimal quality of life is the independence with respect to the bladder and bowel management and sexuality.[9] Some problems that urologists will have to tackle in an adult patient with NLUTD are the consequences of surgical interventions in childhood, such as bladder augmentation or urinary diversion. Due to the underlying pathology, other problems are common – urinary tract infections (UTIs), urinary incontinence (UI), urinary stone disease, and sexual and reproductive issues. These patients might also suffer from the side effects of the chronic use of medicines (e.g., antimuscarinics); however, the literature on this issue is scarce.[10] A regular control allows the identification of risk factors before irreversible changes in the lower urinary tract (LUT) and UUT occur. As Averbeck and Madersbacher recommend,[11] the European Association of Urology (EAU) Guidelines on Neuro-Urology should be followed in patients with congenital NLUTD (Table 1).[12] The adult patient may need help from other specialists, such as a gynecologist, a neurosurgeon, an orthopedist, a gastroenterologist, a psychologist, a physical therapist, or a urotherapist. The interdisciplinary collaboration is necessary not only on the medical but also on social level to enable the patient a full participation in social life.[7,13]

Table 1. Recommendations for the follow-up, according to the European Association of Urology (EAU) Guidelines on Neuro-Urology 2016[12]

Recommendations
Evaluation of the upper urinary tract at regular intervals in high-risk patients.
Physical examination and urine laboratory tests every year in high-risk patients.
Any significant clinical changes should initiate specialized investigation.
Urodynamic investigation as a baseline diagnostic intervention in high-risk patients at regular intervals.

Posterior urethral valve

Posterior urethral valve (PUV) is the most common congenital obstructive uropathy that can lead to ESRD. The incidence of PUV ranges from 1:5000 to 1:8000 births. The severe consequences of the outlet obstruction with regard to the developing bladder include poor compliance, detrusor overactivity and reduced functional volume. Renal hypo/dysplasia can already be diagnosed in utero. However, an accurate prognosis regarding the postnatal bladder and kidney function based on the findings from the prenatal screening is not possible.[14] To avoid or postpone renal impairment, all boys require a close follow-up. While PUV can be successfully managed in children, there are no guidelines on how to follow up adult patients. Holmdahl and Sillén stated that 32% of adult men aged 31–44, treated for PUV in childhood, were uremic, 21% had moderate renal failure and 47% had not been checked since adolescence; there were also signs of bladder dysfunction in 40% of patients.[15] That is why the kidney and bladder function follow-up must be an essential part of the transition. However, an interdisciplinary supervision of the adult "valve" patient is usually not necessary. Nevertheless, regular checks for serum creatinine, blood pressure and the bladder function will help to avoid irreversible changes. If needed, a nephrologist should be involved in the long term.

Exstrophy-epispadias complex

Exstrophy-epispadias complex is a spectrum of genitourinary malformations, ranging from mild epispadias, throughout the classical bladder exstrophy, to the exstrophy of the cloaca. The overall incidence of the EEC spectrum can be estimated at 1 in 10,000 births, with higher occurrence in males as compared to females.[16] Urinary continence and the voiding pattern are mostly evaluated as the end point of the treatment of bladder exstrophy. Woodhouse at el. showed that continence can be achieved in up to 80% of children in highly specialized centers, but only 40% of adults are dry.[17] Furthermore, about 84% of children are able to void, but this function is lost with time in 70% of patients.[17] These are not the only reasons why the EEC patients need attention in adulthood. Those who had surgical bladder augmentation are at risk of metabolic disorders, urolithiasis and

malignancies. The sexual function and fertility are additional issues in adults to be dealt with by urologists and gynecologists. Little is known about the sexual dysfunctions in these populations.[18] In females, fertility is usually maintained (delivery should be by cesarean section), but only 50% of male patients are able to become a father.[19] Due to the anatomical abnormalities of the pelvic ring, the EEC patients may also require the orthopedic care. Patients with the cloacal exstrophy should be treated as NLUTD patients in terms of the bladder management, and they may also need help because of fecal incontinence.[13] Due to the urinary diversion, oncological surveillance is necessary. During the follow-up, the probability of developing a malignant tumor after augmentation cystoplasty is in the range of 0–5.5%.[20] Neoplasia at the anastomosis of the ureters and the colon occurs in about 24% of patients at 20 years of follow-up.[21]

Disorders of sexual development

Patients with DSD are another group requiring a multidisciplinary approach, in many cases starting at birth. Pediatric and adult urologists should provide lifelong, continuous care for the DSD patient in the aspects of reconstruction, sexual function, fertility, and possible lower urinary tract dysfunction (LUTD). In adulthood, female patients are usually supervised by a gynecologist. The gynecological care should cover the newly diagnosed patients (phenotypically female), those who did not undergo reconstruction in childhood and may have complications after feminizing genitoplasty, as well as those who are potentially fertile (limited to congenital adrenal hyperplasia patients).[22] Some DSD patients are at risk of developing gonadal tumors, but the absolute risk of malignancy is unknown.[23] The cooperation of an endocrinologist, a urologist and a gynecologist is crucial in terms of treatment optimization. The psychosexual outcome is important, because the patient's well-being in the long term could be one of the factors determining the decisions regarding indications and timing for the surgical treatment.[24] Urologists and gynecologists are predisposed to offer help and therapy in this area.

Anorectal malformations

Anorectal malformations include a wide spectrum of diseases that affect the anus, the rectum and the urogenital system, i.a., CAKUT. The incidence of ARMs is approx. 1 per 5000 live births. One of the major problems experienced by these patients is fecal incontinence, which requires a follow-up and functional training. This issue should be covered by the surgical team. In some cases, urethral stricture may occur as a result of fistula closure. Furthermore, a number of these patients are at risk of NLUTD. The reason for this is not really known, but these patients require lifelong urological and nephrological supervision. Female patients need gynecological support due to additional abnormalities of the genital tract and possible trouble during pregnancy. For many reasons, they also require concern and help from a psychologist as well as psychosexual assistance.[25,26]

High-volume anomalies with a possible risk for the urogenital tract

Hypospadias

Hypospadias is one of the most common congenital genitourinary conditions (CGCs), affecting 1 per 250 males at birth. This disorder comprises a heterogeneous group of patients. In approx. 70% of them, the urethral meatus is located distally and the defect is not severe, but there are also proximal, more complex cases. The most common urinary complications in patients who have undergone hypospadias repair include meatal stenosis, fistula, urethral stenosis, ventral curvature, UTIs, or lichen sclerosis; these complications may occur many years after the initial surgery. A portion of these patients will present with lower urinary tract symptoms (LUTS), but some might be asymptomatic for a long time.[27,28] The patient requires physical examination and uroflowmetry with postvoid residual measurements. After proximal hypospadias repair, each patient should be examined after puberty, and again as a sexually active man. Unfortunately, there are no standardized questionnaires for the evaluation of the psychosexual function after hypospadias repair for adult patients with a mild hypospadias correction. [27]

High-volume conditions affecting the quality of life

Urinary incontinence

Urinary incontinence is one of the most bothersome signs of LUTD.[29] Approximately 5–10% of schoolchildren suffer from UI, and a low percentage of them do not outgrow it. The majority of patients can be cured by means of standard urotherapy, and the bowel management is often needed as well. Some patients require specific urotherapy (physical therapy, neuromodulation) and pharmacotherapy. Effective therapy depends on a good cooperation between a urotherapist and a urologist.[30,31] Although controversial, an endoscopic intervention is needed in some boys to eliminate intravesical obstruction. The long-term consequences of the invasive treatment are not known, and these patients might be at risk of urethral stenosis and require a proper follow-up.[32] There is a lack of literature on UI in adolescents and on the transition of these patients. Von Gontard et al. hold the view that incontinence in adolescents is a neglected research topic, and that an organized transition process is recommended to improve care in this respect.[33]

Oncology

Adult tumors in children

Renal cell carcinoma (RCC), MiT family translocation renal cell carcinoma (tRCC)[34] and urothelial bladder

cancer[35] are extremely rare in the pediatric population. There is hardly any literature on how to follow up those patients in childhood. Usually, the recommendations from the adult group are used, but the clinical course of those diseases in prepubertal children and adolescents can differ significantly from that observed in the adult population.

Typical pediatric tumors

In recent decades, there has been an increase in the overall survival rate for childhood malignancies. Two out of 3 childhood cancer survivors develop at least 1 late-onset therapy-related complication; in 25% of these patients, the complication is severe or even life-threatening.[36] Based on the Children's Oncology Group guidelines, Bhatia et al. recommended a "shared-care model" that involves both a primary care provider and an oncologist to facilitate the best long-term follow-up.[37] The coordinating physician should select the type and the frequency of visits in cooperation with the oncologist, along with psychological support. Urological tumors may require additional urological and nephrological control (Table 2).[37]

Table 2. Potential late effects of selected therapeutic interventions for childhood cancer by organ/system[37]

Organ system	Potential late effects
Renal	glomerular toxicity tubular dysfunction renal insufficiency hypertension
Bladder	hemorrhagic cystitis bladder fibrosis dysfunctional voiding neurogenic bladder bladder malignancy
Sexual/reproductive (males)	hemorrhagic cystitis bladder fibrosis dysfunctional voiding neurogenic bladder bladder malignancy

Oncofertility

Oncofertility is a field regarding the reproductive future of cancer survivors. The American Society of Clinical Oncology (ASCO) first published guidelines on the preservation of fertility for children and adolescents, and recommended semen cryopreservation for post-pubertal boys before the initiation of therapy. The cryopreservation of the testicular tissue from prepubertal patients and hormonal suppression to preserve the gonadal tissue are still under investigation.[38] Closely cooperating units responsible for particular stages of the process must be created in order to follow the recommendations for the newly diagnosed cancer in a male child or adolescent.

Limitations

The main limitation of the present review is a small number of original and prospective studies related to the topic. Most of the included articles are reviews and expert opinions. Transition into adulthood is becoming an important part of pediatric specialties, which arises from the need to take care of patients whose prolonged life expectancy is a consequence of the development of medicine. For the time being, there are hardly any objective data on this subject in the literature.

Furthermore, only a few urological conditions have been discussed in the review for obvious reasons. Nevertheless, patients with other abnormalities, e.g., undescended testis, primary megaureters and urinary stone disease, might also need a long-term follow-up.

Vesicoureteral reflux (VUR) is a perfect example of an urological problem with a wide spectrum of therapeutic options, from active surveillance, through continuous antibiotic prophylaxis (CAP) and endoscopic procedures, to the most invasive one – ureteral reimplantation. Taking into account the risk factors, the management of VUR should be individualized. Nevertheless, the diagnosis and treatment of VUR are the source of a never-ending debate among pediatric urologists and nephrologists, with the goal remaining the same, i.e., the prevention of febrile UTIs, and thus scarring of the kidneys.[39,40] Although this condition can have severe consequences in the long term, there are no publications on the transition process for those patients.[41]

Conclusions

Children with chronic diseases require a long-term follow-up. Transition of care into adulthood is a challenging issue in all disciplines. The patient, caregivers and healthcare professionals must be all involved in this process. The pitfalls regarding urogenital conditions in terms of transition are as follows:

– there is a wide spectrum of congenital as well as acquired pathologies;

– children are treated in different locations (pediatric urology units, pediatric surgery units, urology units) and all adult patients are referred to urology departments;

– there are different policies/protocols, especially in the case of rare diseases;

– there is a limited number of common teaching activities for pediatric and adult specialists.

Perspectives

The knowledge of transition or rather adolescent medicine should be an additional competence. Recently, it has been gaining more attention, as there is an urgent need to take care of patients who enter adulthood having been

cured from severe diseases. A significant improvement of the healthcare may increase the length and quality of life of such patients. Even in the best-organized centers, a proper transition is successful for only 40% of patients.[42] Transition carries many pitfalls, as mentioned above. Special attention should be paid to cooperation and efficient coordination between healthcare professionals. Multidisciplinary meetings and congresses are needed, but also evaluation and feedback from patients are necessary. In a multidisciplinary approach, medical, social and environmental aspects are taken into consideration. Following the World Health Organization's International Classification of Function, Disability and Health (ICF) model, high-quality care encompasses not only health-related outcomes, but also activities, social participation and environmental factors to address an individual's need to fully function in the society.[43]

Adequate theoretical and practical training of adult urologists interested in taking care of patients with "pediatric" genitourinary conditions must be ensured. The pediatric urologist, in turn, should compile the patient's medical history recapitulation, including in detail all surgical procedures, ongoing health problems, suggestions on the necessary specialist visits, and diagnostic tests. It must be noted that a transition requires a careful approach during a challenging moment of a human life – puberty. All parties must be fully involved to make the whole process smooth and successful.

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