

# The standard of urological consultation of patients qualified for renal transplant – a review

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**Citation:** Antoniewicz AA, Zapala Ł, Bogucki A, Małecki R. The standard of urological consultation of patients qualified for renal transplant – a review. Cent European J Urol. 2015; 68: 376-382.

## Article history

Submitted: Jan. 25, 2015

Accepted: June 23, 2015

Published on-line:

Oct. 15, 2015

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Urological consultation is an important step in the procedure of a patient's preparation before placing him/her on a waiting list for a renal transplant. Urological work-up aims to diagnose, treat, and optimize any preexisting urological disease. In the present paper we present the review of the literature together with the authors' conclusions based on literature and their experience. There is not enough data in current literature and urology manuals on the adequate sequence of the urological management with patients qualified for renal transplant and the literature needs an update. This study presents the crucial steps of the qualification and emphasizes the urge for a more standardized urological approach in patients qualified for a kidney transplantation.

**Key Words:** kidney transplant ↔ urological qualification ↔ kidney failure

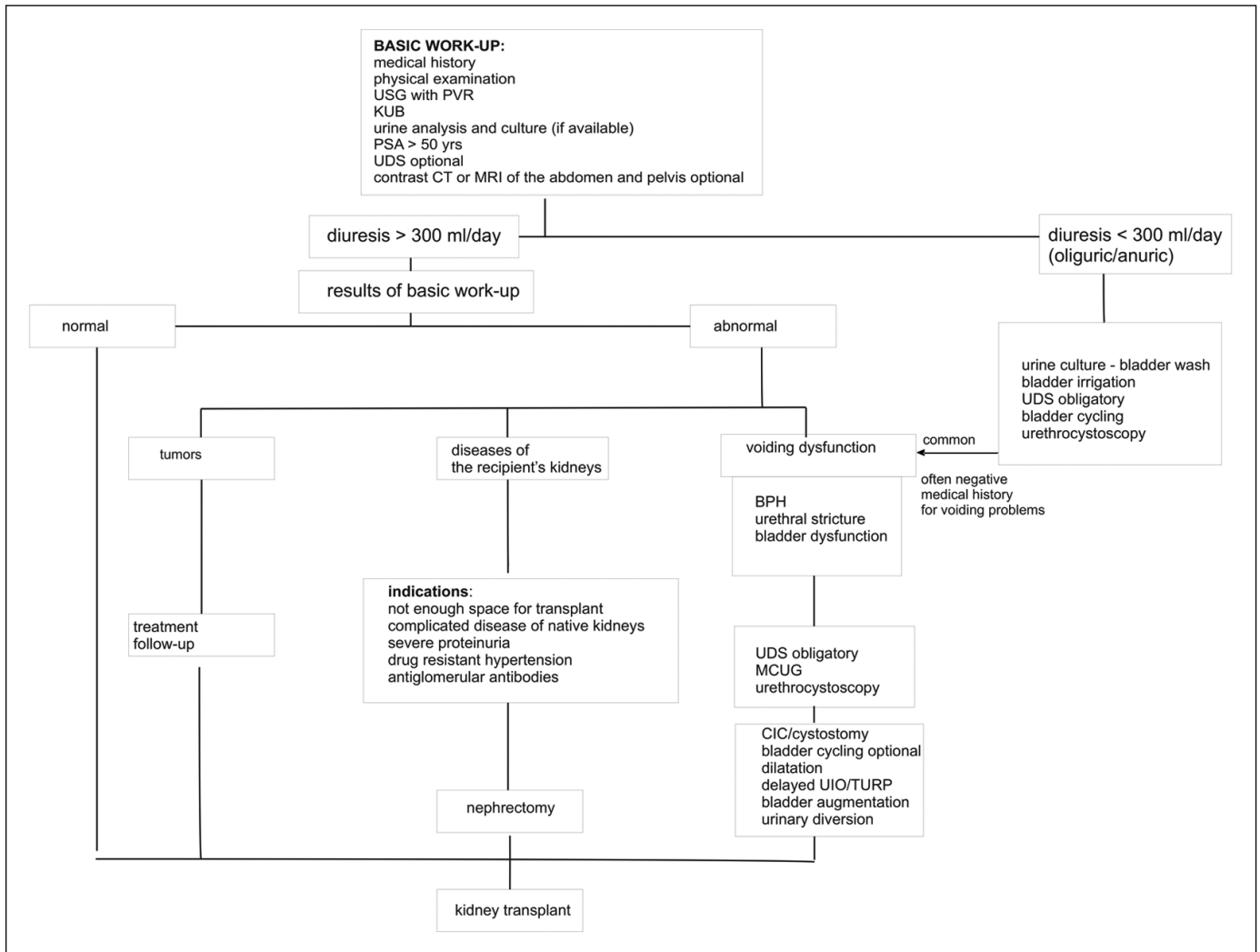
## INTRODUCTION

Renal transplantation is the best known therapy for patients with end-stage renal disease. Chronic pyelonephritis is the primary urological condition in adults which leads to chronic kidney failure, while the urinary tract as a cause of end stage renal diseases is found in 20-25% of pediatric patients and in only 5-7.5% of adults [1, 2]. Furthermore, urinary tract alterations are diagnosed in one-fourth of the transplant candidates [3].

Before being placed on a waiting list for renal transplantation, patients undergo extensive evaluation [4]. Urological investigation is an essential component of this workup. In the review we focus on pre-transplant urological assessment based on literature and their experience coming from consultations in the specialistic uro-nephrology center [5-12].

## Pre-transplant basic urological assessment of the recipient

The basis of a urological work-up prior to the renal transplant comprises of identification, optimization and treatment of any urological condition that would be a contraindication to a successful transplantation. The following rules have to be fulfilled: i) the lower urinary tract should be sterile, continent, compliant and able to store an adequate amount of urine; ii) any malignancies should be ruled out, iii) bladder outlet obstruction should be excluded: normal flow of urine and constant method of bladder emptying *via* own micturition or clean intermittent self-catheterization (CIC) should be documented or urinary diversion if indicated should be performed, and, finally, iv) evaluation for the need for native nephrectomy is also necessary [3, 9].



**Figure 1.** Algorithm for urological assessment prior to kidney transplant. Based on Power et al. [7], modified.

The basic urological evaluation includes taking a systematic medical history (see Figure 1). Some authors claim that this may be conducted without consultation with a urologist, and only the complex cases with abnormal results of basic work-up should be referred to specialists as presented in Figure 1, while others pinpoint that it is always an obligatory step to receive urological opinion prior to enlisting a patient on the kidney transplant waiting list as a result of the national qualification system [5]. The micturition interview may be supplemented with questionnaires assessing the functioning of the lower urinary tract, e.g. International Prostate Symptoms Score (IPSS) or The Kings Health Questionnaire for urinary incontinence [12]. Furthermore, the consultation should take place after having reviewed a patient's bladder diary that records the timing, frequency and volume of voids and any LUTS that appeared together with fluid intake. In the case

of an anuric patient the history focuses on the bladder function before urine production ceased. A physical examination includes systematic assessment of the abdomen and external genitourinary organs together with a digital rectal examination in men. As far as basic work-up is considered it is important to perform both urine examination and culture, ultrasonography of the abdomen and pelvis with a post voiding residual volume calculations. Plain X-ray of the kidneys, ureters, and bladder (KUB) is sometimes used nowadays, while in doubtful cases a CT of the abdomen and pelvis is preferable [13, 14, 15]. Further studies are indicated for patients with a history of urinary tract abnormalities or evidence of pathology on urological evaluation, as additional examinations may be necessary, see Figure 1. Some authors advocate [16], however, that all the candidates for renal transplants should be assessed urodynamically for lower urinary tracts dysfunction.

## Specific screening and management

The specific screening and management of kidney transplant recipients comprises the aspects described below.

### Tumors of the genitourinary system

Seek for tumor in transplant candidates is a serious issue since patients with end stage renal disease are at higher risk for acquired malignancies of the kidney, bladder and some other organs [17]. Screening for the presence of any of the urological cancers in recipients is mainly performed by a DRE and PSA in all men over the age of 50 years [11]. As transabdominal ultrasound is performed in all patients it allows for the exclusions of abdominal masses, with special regard to renal tumors. However, it is well-known that the preferred method of imaging renal cell carcinomas (RCC) are computed tomography (CT) and magnetic resonance (MRI) [18, 19]. If the results of a CT are indeterminate, an MRI may provide additional information by enhancement of renal masses or venous involvement [18]. Patients with reduced renal function are at risk of developing contrast-induced nephrotoxicity (CIN) follow-

ing a contrast-enhanced CT examination with an iodinated contrast agent and patients are also at risk of developing nephrogenic systemic fibrosis (NSF) after a contrast-enhanced MRI with an extracellular gadolinium-based contrast agent [20]. CIN is irrelevant in hemodialysis patients, as the kidneys are already extensively damaged with no important residual renal function to protect. The chance of inducing CIN is greater than NSF in patients suffering from renal impairment, as the prevalence of CIN in patients with GFR <30 mL/min is 40%, and NSF <5% [20]. Finally, all iodinated contrast agents have the potential to induce CIN, whereas NSF can possibly be prevented by using the lowest possible dose of a macrocyclic gadolinium contrast and avoiding repetitive contrast administration within a short period of time. The balance of risk seems to be in favor of the use of contrast-enhanced MRI studies in patients with renal impairment.

It is considered that specific screening for cancers other than specified above is not indicated, provided that there are no indicative medical history data, findings from physical examinations or abnormal basic laboratory results [11].

On the other hand, in individuals with previous malignancy (excluding non-melanoma skin cancer) transplantation is possible after successful treatment with curative intent [17]. In the majority of cases the period of 2 years since cessation of radical treatment may be optimal to perceive that the patient be cured (Table 1) [9]. Even though the 5-year time period would allow the exclusion of most recurrences, it is not suitable in elderly people and seems unnecessary in a great number of cases [17]. In some cases the waiting period has to be specifically defined according to the type, TNM stage and grade of the tumor, together with age and medical condition of the candidate as well. The Israel Penn International Transplant Tumor Registry (IPITTR) from Cincinnati, USA offers a consultation service to medical professionals of the transplant community, which essentially determines the type of tumor and the delay between its treatment and the kidney transplantation ([www.ipittr.uc.edu](http://www.ipittr.uc.edu)). Stratification of the waiting time between 1-5 years according to the type of tumor is presented in Table 1.

**Table 1.** Suggested waiting time for transplantation following successful radical cancer treatment [24, 25, 39, 40]. NMIBC – non-muscle invasive bladder cancer, MIBC – muscle invasive bladder cancer

Tumor type	Suggested minimal waiting time	Additional factors to consider before transplantation
Renal		
incidental	none	recurrence <1% in incidental tumors; overall recurrence 30%; before 2 years 60% recurrence, at 2-5 years 33% and >5 years post transplantation 6%
<4 cm	2-5 years	
>4 cm	5 years	
Wilm's tumor	2 years	should be at least 1 years post completion of chemotherapy
Bladder		
NMIBC	none	high risk local recurrence but low risk of invasive disease;
MIBC	>5 years* (some authors <sup>32</sup> claim 2 years is enough)	carcinoma in situ more aggressive; overall recurrence rate 18-26%
Prostate	2 years	recurrence rate for localized disease: cT1-2- 14-16%; patients with disease outside prostate capsule (cT3) should not be transplanted
Testicular	2 years	recurrence rate 3-12% post-transplant; little data available concerning 2-5-year waiting period

### Renal tumor

It was reported that renal tumors are observed 3.3 up to 9.9 times more frequently in dialyzed patients [21]. There is an elevated risk in patients with end stage renal disease due to adult polycystic kidney disease and nephropathy secondary to chronic non-steroid anti-inflammatory drugs. The recurrence rate for incidentalomas after radical treatment

**Table 2.** Indications for native kidney nephrectomy [11, 12]

the lack of space for kidney transplant
complications of native kidney disease, e.g. chronic pain, infected cysts, ruptured cyst with or without hematuria, urinary tract infections of the renal origin, urolithiasis, suspicion of renal cancer or upper urinary tract cancer
uncontrolled hypertension
uncontrolled nephrotic syndrome
persistence of anti-glomerular basal membrane antibodies

and consecutive transplantation is very low and estimated to be 1% (Table 1), while the recurrence rate of large, symptomatic renal masses reaches 27%. Apart from radical nephrectomy it is sometimes necessary to perform simple nephrectomy, either uni- or bilateral due to benign conditions present in the recipient. It may be both an open or laparoscopic procedure that is usually performed 6 weeks prior to transplantation [12]. There are several indications for native kidney nephrectomy, some of which are presented in Table 2.

#### Prostate cancer

The screening for prostate cancer remains within the basic urological work-up (DRE, PSA) in men >50 years old and biopsy under transrectal ultrasound guidance should be carried out in case of abnormal findings [11]. Even though hemodialysis may affect free PSA measurements, it does not influence total PSA [7]. However, there is no greater incidence of prostate cancer in hemodialyzed patients, and the waiting period of 2 years since radical treatment of localized diseases seems to be reasonable (Table 1). The tendency for a non-delayed transplantation after radical surgical treatment of an organ-confined disease is also documented [22].

#### Bladder cancer

It is estimated that the bladder tumor is 1.4 up to 1.8 times more frequent in dialyzed patients [23]. Non-muscle invasive bladder cancers have low risk of recurrence after transplantation. The consensus was not reached considering the waiting period for muscle invasive tumors, as some authors claim that over 5 years is obligatory [24], while others consider a 2 year-time as enough [23]. It is recommended to act according to the guidelines on bladder cancer, while risk groups (heavy smokers, patients with end stage renal disease due to toxicity, e.g. aristocholic acid, infections or obstructive uropathy, treated with cyclophosphamide, with occupational exposure, with schistosomiasis history) should be screened more strictly (urine analysis, urine cytology, cystoscopy, biopsy) [7].

#### Testicular and penile cancer

Physical examination allows the exclusion of penile cancer, while if there are any doubts concerning the testis, an ultrasound examination is necessary. There is no greater incidence in patients with end stage renal disease having testicular cancer, and recurrence rate is low [7]. On the contrary, it was proved that there is an elevated risk for penile cancer in the transplant population due to human papilloma virus infections [12].

#### Voiding dysfunction

##### Benign prostate hyperplasia (BPH)

It is recommended in BPH patients to complement basic work-up (DRE, urine culture) with complete urodynamic study. The management of uncomplicated BPH should start with medical treatment (alpha-blocker alone or in combination with 5-alpha reductase inhibitor if the gland is over 40 mL). In case of bladder decompensation and elevation of residual volume, an appropriate bladder emptying *via* CIC should be engaged. Surgical treatment should be postponed in oliguric/anuric patients due to the high risk of bladder neck and urethral stricture as a result of “dry urethra syndrome”. The surgical intervention can be safely carried out even in the post-transplant setting with minimal complications and effect on the renal graft function [9]. In individuals, in whom it cannot be delayed, transurethral resection of prostate (TURP) can be performed only when combined with cystostomy, so as to allow for bladder cycling, which is an alternative way to CIC discussed later on.

##### Urethral stricture

Urethral strictures can be idiopathic, traumatic, infectious or iatrogenic in origin and may be observed in all age groups [7, 9]. Medical history and uroflowmetry with post-void residual volume assessment allows for correct diagnosis establishment. In these cases, urethrocystoscopy is recommended, but the management depends on the size and length of the stricture. Instrumental dilatation, direct visual urethrotomy or open urethroplasty are possible ways of surgical treatment, but, again, they should be postponed till the re-establishment of urine output due to the high risk of recurrence.

##### Bladder dysfunction

Many authors claim that only in individuals with medical history or abnormal results of basic work-up suggestive of bladder dysfunction should invasive diagnostic procedures (e.g. voiding cystourethrography, urodynamic study, cystoscopy, ureteropyelography)

be performed [7, 9, 12], while others [16], as stated above, are of the opinion that all potential kidney recipients should undergo proper evaluation of the lower urinary tracts before being qualified for kidney transplantation. Kidney transplant in an individual with abnormal inferior urinary tract requires a close follow-up after the surgery as the existence of bladder dysfunction adversely affects renal graft survival and function. Abnormal bladders (patients with primary vesicoureteric reflux or renal dysplasia, posterior urethral valves, neurogenic bladders, vesico-ureteric tuberculosis, bladder exstrophy and prune belly syndrome) must be assessed urodynamically before kidney transplant, and after the procedure adequacy of urinary drainage must be re-assessed frequently. Crowe et al. concluded that prophylactic antibiotics administered for the first 6 months allow for good results to be obtained with an 89% and 66% one- and five-year graft survival, similar to the cases without urological problems [25].

The criteria of a normal bladder with appropriate tools used for the diagnosis are presented in Table 3 [26, 27].

#### Specific measurements in oliguric/anuric patients

The collection of urine culture in patients with no or low urine output can be difficult. Furthermore, authors argue if and how to perform urine culture in anuric patients. Some advocate that bladder saline wash *via* sterile catheter may be performed and bladder irrigation once a week prior to transplant *via* CIC are advisable as a prevention of symptomatic pyuria [7]. As for urodynamic study, the result of baseline uroflowmetry can be gained in the same way. In oliguric/anuric patients the percentage of lower urinary tracts abnormalities is greater and there is underestimation of bladder dysfunction frequency [28, 29]. One can diagnose those individuals with both anatomic and functional disturbances of LUT.

Following abnormalities: high pressure reservoir, increased residual volume, vesicoureteral reflux, recurrent urinary tract may in turn lead to lost of kidney graft. Renal transplantation performed on a long-term defunctionalized bladder may be carried out but only in carefully selected patients. Furthermore bladder function and continence should be confirmed before transplantation using a program of progressive bladder rehabilitation that is prolonged even for post-transplant period, either *via* suprapubic tube or urethral catheter (bladder cycling, see below) [29]. In long-term defunctionalized bladder atrophy and fibrosis of the mucosa and muscular layer, there can be the formation of a small, high pressure reservoir of low compliance. In these cases ureteral implantation may be challenging and lead to graft lost. However, some authors claim that bladder dysfunction in anuric patients is temporary and rehabilitation is fast and uneventful. According to Chun et al. similar to patients with a normal bladder size, renal transplantation can be successfully implemented in patients with a small bladder and the bladder capacity does not need to be increased in pre-transplant rehabilitation [30].

Bacteriuria is a common finding, however, long-term prophylaxis in patients on CIC is not necessary provided that they are asymptomatic [31]. Patients with neurogenic high pressure bladders should be treated with anti-cholinergic drugs with regular post-void residual volume assessment together with CIC every 2-3 hours if needed [9]. It is important to teach patients how to perform CIC properly long enough prior to kidney transplant. However, in individuals who are not able to perform CIC, cystostomy or urinary diversions (conduit, pouch or bladder augmentation) are other options.

#### Clean intermittent self-catheterization

Clean intermittent self-catheterization allows for safe transplantation provided it is performed properly, even in individuals with abnormal lower urinary tracts. The main conclusion of the urological consultation is that only patient with sterile continent and low pressure urine reservoir that is emptied in a safe and repeatable manner can be adequately qualified for transplant [7]. It can be done either *via* CIC or urinary diversion. In the paper by Gill et al. the serum creatinine concentration assessed after one and three years since surgery, the length of hospital stay, the overall number of graft rejections and amount of people that remained professionally active were similar when compared individuals managed by urinary diversion or CIC [32]. Even though CIC may cause more complications in patient on immunosuppression when

**Table 3.** Criteria of normal bladder. Based on [28, 29], modified

Criteria	Adults	Children	Tools
Bladder capacity	350-650 ml	(age/2+6)x28,35	Bladder diary Urodynamic study
Bladder Compliance	>30 ml/cm H <sub>2</sub> O	>30 ml/cm H <sub>2</sub> O	Urodynamic study
Sterility	Urinary tract infection > 10 <sup>5</sup> CFU/ml from midstream urinalysis		Urine culture
Ability to empty	Men <40 yrs Qmax >25 ml/s Men >60 yrs Qmax > 15 ml/s Women >30-35 ml/s		Uroflowmetry
Residual volume	<20 ml		Transabdominal ultrasound



compared to healthy people it seems a better way of management than urinary diversion due to the simplicity, positive psychological effect and similar morbidity to other forms of treatment.

### Bladder cycling

In oliguric patients (<300 ml/day) a bladder cycling is a useful way of preventing bladder dysfunction. It can be done *via* cystostomy: the patient fills the bladder with saline til urgency and leaves the fluid inside for 30 minutes [33]. Subsequently, a voiding occurs and post-void residual after opening the cystostomy is assessed. Bladder cycling may help to distinguish, if high pressure bladder is a result of dysfunction or preexisting disorders and indicates the adequate surgery for correction. Furthermore, it increases bladder capacity and may be a treating tool [10].

### Functional urethroscopy

Since the ultrasound in anuric patients misses the bladder assessment, it is urethroscopy that can be implemented. Another supplementary procedure to urodynamic study role is functional urethroscopy. It may be performed either using rigid (females) or flexible (females and males) endoscopes. The crucial steps of the functional cystoscopy are: i) implementation of local anesthesia *via* urethra, ii) bimanual examination, iii) insertion of the cystoscopy and slow filling of the bladder (50 ml/min) with warm fluid to assess first sensation, first and strong desire to void and, finally, urgency so as to assess functional capacity of the bladder; it is followed by bladder emptying *via* micturition and residual volume assessment using catheter; in female patients or in post-prostatectomy patients a cough test at a capacity of 250 ml/maximal volume can be performed, iv) routine urethroscopic assessment.

### Urinary diversion

Several doubts remain about the safety and efficacy of renal transplantation for patients with primary urological abnormalities [3]. If there are contraindications for implantation of the ureter and kidney to the recipient's bladder, several strategies are possible. Urinary diversion – either conduits or continent pouches that need catheterization – are one of the options in case of sphincter deficiency (e.g. neurogenic bladder). In case of bladder of low compliance with normal sphincter, bladder augmentation or continent pouch are possible alternatives [34, 35, 36]. The majority of urologists prefers to perform pre-transplant urinary diversion within 10-12 weeks, however both augmentation and conduits can be made in the post-transplant period, but all these patients are at a greater risk of infection.

## CONCLUSIONS

A thorough evaluation of the urinary tract is a mandatory step to avoid unforeseen problems occurring after kidney transplantation. There is not enough data in current literature and in urology manuals focusing on the adequate sequence of the urological management with patients qualified for renal transplant. As a result, it seems to be justified to reconsider the subject of urological evaluation prior to a renal transplant in terms of increasing numbers of patients' qualified for living donation and strict cooperation with transplantologists, nephrologists and urologists. The steps of an appropriate urological assessment, which were summarized in Figure 1, should be familiar to all urologists, together with the adequate management of pre- and post-transplant urological conditions.

### CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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