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REVIEW

Urodynamics in the Transplant Population

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Abstract

Purpose of Review Urodynamic testing (UDS) is a valuable tool for understanding the safety of the lower urinary tract (LUT). The goal of this review is to provide evidence-based indications for use of UDS in both the pre- and post-kidney transplant (KT) settings.

Recent Findings Pre-transplant bladder cycling with UDS for anuric or oliguric patients is no longer recommended. Instead, UDS aids in identifying LUT anomalies that may require optimization prior to transplant, especially in patients with known urologic etiologies of end-stage renal disease (ERSD). In pre-KT patients with recurrent urinary tract infections (UTIs) or prior urologic/pelvic interventions, UDS should be used judiciously when the etiology of LUT dysfunction is unclear. In the post-transplant setting, urologists are often consulted for LUT symptoms (LUTS), hydronephrosis, urinary retention, declining renal function, and most commonly, recurrent UTI. Again, UDS should not be routinely performed first line, but as an adjunct to distinguish similarly presenting LUT etiologies such as bladder outlet obstruction (BOO) and bladder dysfunction.

Summary UDS remains the gold standard for characterizing the LUT, and when utilized appropriately, can identify factors promoting graft and patient survival after KT.

Keywords Urodynamics · Kidney transplant · Lower urinary tract dysfunction · Recurrent urinary tract infection

Introduction

According to the Organ Procurement and Transplant Network as of October, 2023, over 20,000 kidney transplants occur in the USA every year. While a majority of these operations are now performed by transplant surgeons, urologists are frequently consulted pre- and post-transplant to evaluate genitourinary factors that may affect graft survivability [1].

UDS is defined by the International Continence Society as a series of non-invasive and invasive diagnostic tests that measure physiologic parameters relevant to the function of the LUT (Table 1) [2•, 3–5]. UDS provides a significant amount of data regarding the safety of the LUT, and it is important to understand the proper indications for its use in transplant patients. In both pre- and post-KT settings, the goal of UDS is to optimize the LUT for renal allograft survival. When accessible, fluoroscopic (also known as "video") UDS is highly preferred to diagnose anatomic abnormalities such as vesicoureteral reflux (VUR), hydronephrosis, trabeculations, and bladder neck obstruction [6]. As a rule, UDS should be utilized *to answer a specific clinical question* and not as a ubiquitous diagnostic test among KT patients.

The purpose of this review is to provide up-to-date evidence behind the utility of UDS in the pre- and post- KT population and promote evidence-based use of this limited resource in clinical settings.

Pre-Transplant Evaluation

According to the American Urological Association (AUA), UDS is not routinely indicated prior to KT and should be selectively performed for urologic etiologies of ESRD, recent/recurrent UTIs, or in the setting of previous urologic interventions [7, 8]. In 2023, Kennedy et al. published a retrospective review of 789 KT patients at a single academic institution to identify factors associated with urological complications and patients that may benefit from closer pre-transplant evaluation including UDS [9]. Corresponding to

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Table 1 Components of urodynamics

Exam	Data
Non-invasive	
Uroflowmetry	Voided volume
	Flow rate
	Maximum flow rate
	Average flow rate
	Voiding time
	Flow time
	Time to maximum flow
	Uroflow curve
Post void residual (PVR)	PVR
Invasive	
Cystometrogram	Filling pressure
	Sensation
	Involuntary contractions
	Compliance
	Capacity
Pressure/flow studies	Detrusor pressure
	Flow rate
Urethral pressure studies	Urethral closure pressure
	Maximum urethral pressure
	Maximum urethral closure pressure
	Functional profile length
Electromyography	Pelvic floor muscle activity
	Striated urethral sphincter activity
Videourodynamics	Fluoroscopy

AUA recommendations, patients with recurrent UTIs, history of prostate cancer, benign prostatic hyperplasia (BPH), and prior prostate surgery were more likely to develop post-transplant infection and obstruction.

Researchers have attempted to define the appropriate, high-yield pre-KT population that would benefit from UDS testing. For example, Tangpaitoon et al. recently looked at factors associated with low compliance bladders to identify clinical predictors for urodynamic evaluation [10]. Of 152 ESRD patients prospectively recruited to undergo UDS, 94 were found to have normal bladders and 58 had low-compliance bladders. Low-compliance bladders were associated with diabetes status, renal replacement therapy duration, and daily urine output. According to this model, patients with high scores based on risk factors have a higher risk of low-compliance bladder, and thus are recommended to undergo UDS prior to KT.

However, it is important to acknowledge that incidental LUT dysfunction is common in patients with ESRD, even when of non-urologic etiology. Zermann et al. performed screening UDS on 52 patients undergoing evaluation for KT and found abnormalities in 77% of patients including bladder hypersensitivity, poor compliance, detrusor instability, and detrusor-sphincter dyssynergia [11]. The clinical significance and impact in management of these findings remain poorly understood, and often become inapplicable data points in the clinical setting if indiscriminately obtained.

In this section, we aim to summarize recommendations for pre-KT LUT evaluation with UDS (Table 2).

Defunctionalized Bladders and Bladder Cycling

Diabetes and hypertension are the most common causes of chronic kidney disease (CKD) and ESRD worldwide. Although the majority of patients undergoing KT do not have primary urologic pathologies, poor bladder capacity (< 100 mL) and compliance (< 10 mL/cmH$_2$O) can be found in 14–34% and up to 32% of ERSD patients, respectively, and are directly associated with length of anuria [12–17]. Historically, urologists have explored the concept of bladder rehabilitation through bladder cycling, in which continuous bladder irrigation is up-titrated over several days [18]. The purpose is to mimic normal urinary flow so that the function of chronically contracted bladders can be assessed via UDS. This is no longer widely practiced as studies have consistently shown that kidneys can be safely transplanted into defunctionalized bladders (DB), which regain normal capacity and compliance within 1 year of KT [19–21].

Table 2 Pre-transplant indications for UDS

Population	Indications
Bladder cycling for anuric/oliguric patients	Not indicated
Urologic etiologies of ESRD	Congenital anomalies of the kidney and urinary tract Assess safety of LUT for KT After intervention for optimizing LUT for KT
Recurrent UTI	Not routinely indicated Concern for LUT abnormality of unclear etiology
Prior urologic intervention	Not routinely indicated Concern for impaired bladder compliance *For example, hydroureteronephrosis, incomplete bladder emptying, recurrent UTI, and/or severe incontinence*

Contemporarily, in 2018, Neves Neto et al. biopsied bladder mucosa and detrusor samples in 33 patients with defunctionalized bladders and 35 patients with normal bladders (diuresis < 300 vs. > 300 mL/24 h) to compare receptor mRNA levels commonly altered in LUT dysfunction [22]. Apart from a 2.8-fold overexpression of the α_{1D} adrenergic receptor ($p = 0.018$) in the defunctionalized bladder cohort, there were no other statistically significant differences in gene expression. Of clinical relevance, no significant differences in quality of life (QOL) or symptom scores were found among the two cohorts. Most recently in 2023, Osman et al. performed a randomized controlled trial (RCT) comparing clinical outcomes in patients with DBs (< 100 mL capacity) who underwent KT with ($n = 23$) and without ($n = 20$) prior bladder cycling [23]. No significant difference in objective urodynamics measures such as capacity ($p = 0.3$), compliance ($p = 0.4$), contractility ($p = 0.2$), and maximal detrusor pressure ($p = 0.8$) was found. Although it did not reach statistical significance, rates of urinary tract infection (UTI) admissions were lower in the bladder cycling (35%) versus control (60%) group in this small cohort ($p = 0.09$). No significant differences in intraoperative difficulty of ureterovesical anastomosis were found ($p = 0.3$).

Affirming research published since the 1970s, novel studies continue to demonstrate comparable molecular, as well as clinically objective and subjective outcomes in patients undergoing KT with or without bladder cyciling [24–26]. Thus, bladder cycling and UDS for evaluating bladder function in long-term dialysis patients with anuria or oliguria are not warranted.

Urologic Etiologies of ESRD

Urologic etiologies of ESRD are most commonly encountered in those with congenital anomalies of the kidney and urinary tract (CAKUT). Individuals with CAKUT represent 29–40% of pediatric ESRD and include aplasia/hypoplasia/dysplasia, medullary cystic disease, multicystic-dysplastic kidney, neurogenic bladder, obstructive uropathy, reflux nephropathy, and vesicoureteral reflux (VUR) [27, 28]. Over the years, research has demonstrated no significant difference in long-term graft survivability for patients with CAKUT, including those who have undergone urinary tract reconstruction [29–32]. However, this is in part due to a thorough pre-transplant evaluation that ensures the graft is being transplanted into a low pressure LUT system that empties efficiently [33].

According to Evans-Barns et al., UDS is widely incorporated in the initial work-up of pediatric candidates with maintained urine output to ensure adequate bladder function prior to KT [33]. In any patients with known or suspected CAKUT, fluoroscopic UDS should be performed to identify any need for optimizing interventions prior to KT, which can improve long-term graft outcomes [34]. Such interventions may include anticholinergic or beta-3 agonist medications, initiation of clean intermittent self-catheterization (CIC), onabotulium toxin injection, and/or surgical procedures to improve bladder storage capacity and compliance (e.g., bladder augmentation) with or without alternative drainage in the form of a catheterizable channel [35]. Incontinent urinary diversions such as ileovesicostomy or ileal conduit diversion may also be considered in select patients. One detailed protocol for bladder evaluation and optimization prior to KT at a tertiary center was recently published in 2023 by Mariotto et al. [36] In patients without urinary diversion (e.g., ureterostomy or vesicostomy), UDS was initially performed to assess safety (Pdet < 30 cm) for bladder transplantation. Patients with low compliance/capacity (< 65% expected bladder capacity) or detrusor overactivity (DO) were treated with anticholinergics, CIC, and botulinum toxin A (BtA) injections, then re-evaluated with repeat UDS. Diverted patients were un-diverted if feasible with a suprapubic tube (SPT), then administered BtA and bladder cycling with saline for 4 weeks. Half (5/10) of this cohort was found to have adequate bladder function on UDS evaluation and did not require bladder augmentation prior to KT. Finally, anuric patients similarly had SPT placement followed by BtA injections and bladder cycling. Ultimately, this protocol allowed for 57% (20/35) of patients to successfully undergo KT into their native bladder.

In 2021, Kim et al. looked at the impact of LUT investigations, including UDS, on transplant outcomes among patients with non-urologic and urologic etiologies for ESRD [37]. Thirty percent (29/97) of the urologic ESRD cohort underwent UDS, and 14% of these studies resulted in interventions. When UDS was performed in non-urologic ESRD patients (11/227), no changes in management were reported. Of note, routinely ordered UDS (initial or repeat) without specific clinical concern changed management in 0% of the non-urologic (0/2) and 8% (1/13) of the urologic cohort. Therefore, patients with known urologic etiology of ESRD should undergo UDS if there is any question of the donor kidney being transplanted into a safe LUT, and any LUT-optimizing interventions should then be followed by interval UDS. This being said, patients in this cohort have often undergone extensive work-up throughout their lifetime and care should be taken to prevent unnecessary repeat examinations, including UDS.

Recurrent UTIs

Many sources, including the AUA, recommend that patients with recurrent UTIs should undergo evaluation prior to KT [7, 38•, 39]. However, recurrent UTI and the patient populations to which this recommendation applies are not well defined. According to the AUA guidelines for recurrent uncomplicated UTI in women, UDS should only be performed when there is clinical suspicion of an anatomic or functional abnormality of the urinary tract [40]. For women with recurrent UTI planning to undergo KT, we agree with following the AUA guidelines and only performing UDS in patients with complicated UTI or in those in whom anatomic or functional issues are suspected. In pediatric populations, VCUG is indicated in the setting of recurrent febrile UTIs and/or abnormal renal bladder ultrasonography (US) [41]. It is the opinion of the authors that recurrent UTI work-up in transplant candidates should reasonably mirror that performed in the general population.

Prior Urologic or Pelvic Interventions

Patients who have undergone prior urologic or pelvic interventions such as surgery or radiation therapy, and present with recurrent UTIs, incomplete bladder emptying, unilateral or bilateral hydronephrosis, and/or severe urinary incontinence should be evaluated for LUT dysfunction as these could be signs of impaired bladder compliance. There exists a paucity of data surrounding the utility of UDS and outcomes of KT in this population. This is perhaps a result of the discrepancy in the mean age of KT (44) and pelvic interventions that can lead to BOO such as radical prostatectomy, anti-incontinence surgeries, and pelvic radiation for various malignancies, which typically occur in the 5th to 7th decades of life [42–45]. In non-KT patients, a systematic review of post-radiotherapy prostate cancer patients by Yao et al. in 2021 found significantly reduced bladder capacities compared to non-radiated patients, as well as impaired bladder compliance in 18.8–62.5% and de novo DO in 13.3% of patients [46]. The significance of these UDS findings on outcomes or management is unknown. Similarly, Aponte et al. looked at 54 women with elevated post-residual urine volume secondary to anti-incontinence surgeries and found no difference in symptom improvement or success of intervention in the UDS and no UDS cohorts [47]. Nevertheless, the average age of KT is rising and as the population of KT candidates progressively overlaps with patients with prior urologic interventions, further studies will be warranted to define the role of UDS in this group [48].

Post-Transplant Evaluation

Akin to the pre-transplant setting, UDS can be utilized post-transplant to identify high-pressure LUT systems which increases risk for upper tract injury [49]. Patients can present with various signs and symptoms of LUT dysfunction including bothersome LUTS, hydronephrosis, urinary retention, worsening renal function, and/or recurrent UTI [50]. One large single-institution series of over 4000 KT patients reported VUR (which can be a physiologic sequela of refluxing anastomosis) and ureteral stricture as the most common anatomic urologic complications following KT [51]; however, recurrent UTI (including pyelonephritis) is the most common indication for referral to a urologist post-transplant. While ureteral strictures are primarily identified via retrograde pyelography, videourodynamics or VCUG is used to diagnose VUR. Additionally, UDS can identify risk factors for recurrent infection or graft dysfunction such as poor bladder compliance or incomplete emptying as a result of BOO, detrusor underactivity, or both. In the general population, BOO is frequently due to benign prostatic hyperplasia (BPH) or urethral strictures in men and anti-incontinence procedures in women [52]. According to the AUA white paper on non-neurogenic chronic urinary retention, UDS should be considered if interventional management is indicated or if poor bladder compliance (< 15 mL/cm H2O) is suspected [53].

Bothersome LUTS can be suggestive of storage, voiding, and post-micturition abnormalities, and may also be potentially detrimental to the graft kidney and the patient's QOL [54]. As outlined by the AUA and the European Association of Urology, the initial work-up of LUTS in males and females consists of a thorough history and physical exam, symptom score, bladder diary, and urinalysis [55, 56]. Non-invasive urodynamic measures, such as flowmetry and PVR, can also be obtained. In agreement with the aforementioned guidelines, UDS can be utilized at the discretion of the treating urologist based on the degree of symptoms, diagnostic uncertainty, and/or lack of improvement with conservative therapies.

In the non-KT popupation, an RCT performed across 26 hospitals in England randomized 820 men seeking potential intervention for bothersome LUTS to UDS or standard care and found UDS did not impact surgical rates [57]. However, in one study by Righetto et al., researchers retrospectively looked at 233 male KT patients > 50 years of age to investigate the role of UDS in diagnosing BOO in this population [58]. Thirty percent (71/233) of patients developed lower urinary tract symptoms (LUTS) and 73% of these patients (52/71) underwent UDS. The authors report that UDS was instrumental in differentiating LUTS due to BOO as opposed to other pathologies, thus identifying the appropriate candidates for transurethral resection of the prostate (TURP). Of the 51 patients, 31% did not demonstrate BOO on UDS, were treated medically, and did not require downstream TURP long term.

In relation, all of the above findings may be associated with UTI, which is the most common infectious complication seen (45–72%) in post-KT patients [59–61]. Recurrent UTIs can increase the risk for antibiotic resistance, stone formation, and possibly poorer patient and graft survival, and thus must be evaluated thoroughly [62–64]. An algorithm published by Mitra et al. indicates video UDS for work-up of bladder dysfunction, BOO, or vesicoureteral reflux (VUR) after structural abnormalities have been ruled out by US and computed tomography (CT) [65]. In a contemporary retrospective review, Halskov et al. looked at 571 KT patients between 2014 and 2021 to identify the incidence of recurrent UTIs and associated risk factors in order to understand impact on patient and graft survival [66]. In this Denmark cohort, 18% had recurrent UTIs, defined as ≥ 3 culture-verified UTIs within a year. Fifty-five percent (57/103) of these patients were referred for urologic work-up and 21% underwent UDS. Unfortunately, it is unclear what influence, if any, UDS had on management.

The long-term impact of recurrent UTI on graft survival remains unclear and has been reviewed by Hollyer et al. [67] Although many studies report negative effects on graft and/or patient survival outcomes, some studies demonstrate no clear association [68–70]. Nevertheless, it is clear that recurrent UTI can lead to significant morbidity to varying degrees, including urosepsis, bacteremia, decreased renal function, need for re-operation, and acute cellular rejection. Given potentially higher consequences of recurrent UTI in KT patients, it is the opinion of the authors that a lower threshold for utilizing UDS is acceptable in this population. Particularly, UDS may be helpful in the following settings: unclear etiology after initial evaluation with non-invasive testing, patients with more than one episode of pyelonephritis or urosepsis, worsening renal function, and/or evidence of obstruction including hydronephrosis and elevated PVR. In the clinical experience of the authors, work-up for recurrent UTI in post-KT patients is often unrevealing despite extensive testing, including UDS, and clearly represents an area in need of additional research. However, a thorough and tailored evaluation ensures the highest likelihood of identifying the proper therapeutic intervention. Of importance, given elevated risk of UTI and pyelonephritis, it is recommended that KT patients receive antibiotic prophylaxis when undergoing UDS [71]. Indications for post-KT UDS are summarized in Table 3.

Table 3 Post-transplant indications for UDS

Population	Indications
LUTS	Unclear etiology *For example, BOO vs. bladder dysfunction* Severity of symptoms Lack of improvement with conservative therapies
Recurrent UTI	Unclear etiology > 1 episode of pyelonephritis or urosepsis Worsening renal function Evidence of obstruction *For example, hydronephrosis, elevated PVR*

Future Directions

In the preoperative setting, UDS plays a critical role in optimizing the LUT for transplant in patients with CAKUT or those with known urologic issues such as BPH leading to retention [72]. However, it is uncertain if other indications for pre-transplant UDS including recurrent UTI and prior urologic interventions should differ from that for the general population. Antoniewicz et al. recommends UDS in all patients with BPH undergoing work-up for transplant, which does not reflect standard practice in the general population [73]. Although transplant patients represent a higher-risk population, it is unclear if liberalized use of UDS impacts outcomes or management. Similarly, in the post-transplant setting, there lacks sufficient evidence to support a lower threshold for UDS use in transplant patients with signs and symptoms of obstruction and/or recurrent UTI than in non-transplant patients. UDS can be difficult to access in resource-limited settings. Even in large academic centers, UDS appointments are limited by time and resources. Further efforts to create evidence-based guidelines on UDS use in KT patients are required. Finally, in regard to technique, contrast-enhanced voiding urosonography (ceVUS) is emerging as a comparable, radiation-sparing, and more comfortable alternative to fluoroscopic UDS in the pediatric population [74–76]. Future studies will be required to determine its efficacy in evaluating transplant patients.

Limitations

This review was not conducted systematically and is open to potential bias. Most of the studies referenced in this paper consist of single-institution, retrospective data and may not comprehensively represent all evidence for UDS in KT patients.

Conclusion

In pre-KT patients with CAKUT, recurrent UTI, and/or prior urologic interventions, UDS can aid in identifying LUT abnormalities requiring optimization prior to transplant. In post-KT patients, UDS serves as an adjunctive tool for assessing patients with recurrent UTI or incomplete emptying due to outlet obstruction or voiding dysfunction. Formulating a specific “UDS question” derived from careful history taking and non-invasive testing is a tenant of good UDS stewardship [77•]. This principle should be adhered to so that UDS, a limited resource, is not mis- or overused in the KT population.

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Declarations

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