



Bladder Augmentation Surgery in Prospective Renal Transplant Recipients - A Nephrologist Perspective

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Abstract

Extrapolating success of Bladder Augmentation Surgery (BAS) in pediatric renal transplant population to adult renal transplantation program could be a challenging action; but it would open up an option for adult end stage renal failure patients resulting from lower urinary tract abnormalities, who are otherwise contraindicated from transplant surgery. Currently a platform of BAS has been developing as predicted by a significant number of papers based on this innovative and courageous maneuver, that are being published in current renal transplant and related literature.

The definition of BAS in the context of renal allograft, and characterization in adult renal transplant are yet to be précised in terms of indications, selection of surgical technique and transplant subjects, and defining post-transplant outcome in short term and long term complications, graft function and survival in addition to its' socioeconomic impact. The methodology of BAS is nonetheless not more complex than that of other sophisticated urological surgical procedures as practiced in related urological issues. The complexities associated with BAS may be the major litigating factor though, the success of BAS in pediatric transplant with its time tested relevance, could be a motivation to practice this challenging procedure in otherwise contraindicated adult renal transplant. Moreover, the need for a centralized guideline is also felt in recent years as more and more interests have been being shown worldwide. In this context current status of BAS in adult renal allograft surgery needs to be defined and would be of significant importance in clinical transplantation. This review aims to bring the essence of BAS in adult renal transplantation to the renal physicians in a legible format.

Keywords: Bladder augmentation surgery; Renal Transplant; Nephrologist

Introduction

Although Bladder Augmentation Surgery (BAS)–known as urinary Bladder Cystoplasty (BC) - in adult endstage renal failure patients going for elective renal transplant (RTx) is virtually uncommon and rarely practiced currently, a nephrologist would be in a remarkably unfamiliar zone dealing with such cases [1]. It would be of interest to the nephrologist's perspective to get a renewed acquaintance in that subject. The aim of this review is mainly to focus on such unfamiliar and hitherto unrecognized situation post renal transplant. Bladder augmentation surgery or bladder cystoplasty is done mainly to reconstruct a structurally or functionally reduced bladder volume either due to congenital or due to acquired bladder defects [2]. It is common in pediatric urology and non-transplant adult urological surgery. In pediatric renal transplantation bladder cystoplasty is done in End Stage Renal Failure (ESRF) as a result of congenital urogenital malformation with obstructive uropathy including neurogenic bladder [3]. The cystoplasty is accomplished either as Enterocystoplasty (EC), where a patch of small intestine is auto-grafted to the bladder, or as Ureterocystoplasty (UC), where the native ureter of a non-functional endstage kidney is used to increase the size of the contracted urinary bladder. Both types of surgery have its own merits and demerits.

However, the issues in terms of structural and metabolic complications in the long run may be notably compromising the overall outcome. This needs to be understood by the nephrologist as well as the receiving patients. Therefore a renewed understanding of the relatively unfamiliar subject from the nephrologist's perspectives is of paramount importance.

Indication of Bladder Augmentation Surgery

A brief review of the indications of BAS can be stratified in pediatric group and adult patients. In both age groups BAS has indications in non-transplant conditions and transplant surgery (Figure 1 and Table 1).

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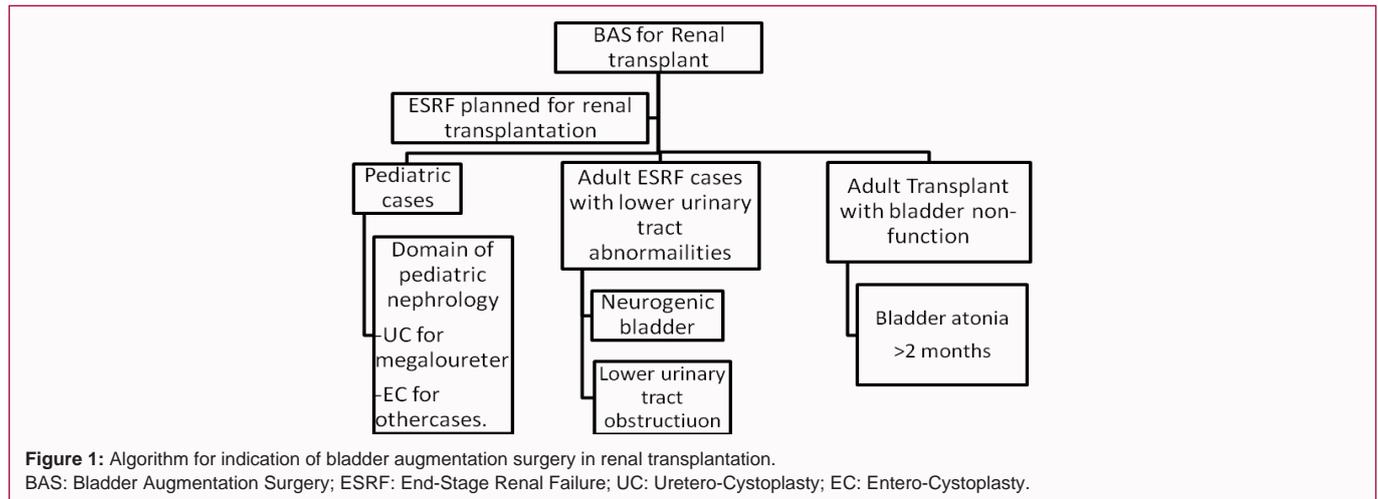


Table 1: Causes of ESRF requiring BAS related to non-transplant conditions, and related to renal transplantation.

Conditions requiring BAS	Pediatric transplant	Adult transplant	Types of BAS requirement
Neurogenic bladder. (With or without ESRF)	1. Congenital i.e spina bifida	1. Acquired from spinal trauma	Yes; EC (Transplant related & Non-transplant related)
Congenital lower urinary anomalies. (With or without ESRF)	1. Congenital VUR, 2. Exstrophy of bladder, 3. Epispadias, 4. Hypospadias, 5. Congenital neurogenic bladder.	1. Congenital VUR, 2. Congenital neurogenic bladder. 3. PUJ obstruction.	Yes; EC (Non-transplant related) UC (Transplant related when there is megaloureter)
Obstructive uropathy due to congenital cause with ESRF.	1. Posterior urethral valve.	1. PUJ obstruction. 2. BPH	Yes; UC Transplant related
Acquired defects- Non-neurogenic bladder	As in adults	1. Interstitial cystitis, 2. Schistosomiasis, 3. Tuberculous cystitis, 4. Interstitial cystitis/bladder pain syndrome, 5. Post radiation cystitis 6. Cystitis associated with systemic or intravesical chemotherapy	Yes; EC for non-transplant related. UC for transplant related.
Acquired defects-Neurogenic bladder		Failed conservative treatment: 1. Spinal cord injury and 2. Spinal cord diseases including multiple sclerosis. 3. Detrusor muscle over activity.	Yes; EC for non-transplant related. UC for transplant related.
Post-transplant BAS		1. Bladder atonia failed to adapt after transplant surgery.	Yes; EC as ureter are normal mostly.

(BAS: Bladder Augmentation Surgery, ESRF: End-stage Renal Failure, VUR: Vesico-ureteric Reflux; PUJ: Pelvi-ureteric Junction; BPH: Benign Prostatic Hypertrophy; UC: Uretero-cystoplasty; EC: Entero-cystoplasty, EC is done by harvesting a segment of small intestine, UC is done by harvesting dilated native ureter)

Indication of BAS for pediatric non-transplant

Indication for BAS for non-transplant related conditions is to create a low pressure but high volume urine reservoir. This permits a notably improved continence and voiding, at the same time helps to maintain function of upper urinary tract including integrity of kidney. This helps preserving good renal function. The situations where the BAS is required are congenital Vesico-Ureteric Reflux (VUR), exstrophy of bladder, epispadias, hypospadias, posterior urethral valve and congenital neurogenic bladder. In these conditions EC is done mostly, by harvesting a segment of small intestine. This allows fairly adequate amount of surface area with mucosal integrity [4,5].

Indication of BAS for pediatric renal transplantation

In pediatric renal transplantation, BAS has opened up the scope of transplantation in ESRF caused by congenital neurogenic bladder and congenital urinary abnormalities leading to obstructive uropathy. Not until a few decades ago, transplantation was denied in such situations [6,7].

Indication of BAS for adult non-transplant

In adult non-transplant situations BAS remains a viable option in both neurogenic and non-neurogenic bladder dysfunction where conservative approach, pharmacological therapy and minimally invasive surgeries have failed to show adequate response, and have been shown to be unsuccessful and exhaustive [8]. Non-neurogenic bladder is associated with infective and inflammatory disorders of bladder. These include, interstitial cystitis, schistosomiasis, tuberculous cystitis, interstitial cystitis/bladder pain syndrome, post radiation cystitis and cystitis associated with systemic or intravesical chemotherapy [9,10]. In these conditions enterocystoplasty is done instead of ureterocystoplasty to maintain an intact upper urinary tract. The non-transplant related BAS for neurogenic bladder refractory to treatment is resorted to conditions associated to spinal cord injury and spinal cord diseases including multiple sclerosis. Patients with detrusor muscle over activity, who fails conservative measures with anticholinergic medications, trial of intravesical botulinum toxin and sacral neuromodulation, are considered for BAS with EC [11,12].

Indication of BAS in adult renal transplant patient for non-transplant reasons

BAS for adult renal transplanted patients is more confined to a fewer conditions including neurogenic and non-neurogenic bladder. In a smaller proportion of adults, lower urinary tract structural abnormalities causes ESRF that requires consideration for BAS before renal transplantation. These groups of patient have had their bladder abnormalities as mentioned above in childhood. But their Chronic Kidney Disease (CKD) had reached ESRF requiring renal replacement therapy in adult life. In one study less than 0.5% (24 out of 1406 transplant) of adult transplant population had undergone BAS with EC before renal transplant surgery with a mean interval of 9.2 (6.5-17) months between BAS and RTx [13].

Indication for BAS in adults for transplant related reason

Adults do not require BAS post renal transplant commonly, as most transplants are done within reasonable time lapse after reaching ESRF in most cases of living donor related renal transplant patients. In disease donor related renal transplant we did not encounter any requirement for BAS post-transplant in our center. However, the occurrences of dysfunctional bladder after prolonged anuric state during dialysis requiring period of ESRF (more than 2 years) could pose a significant risk for post-transplant urinary retention. This is due to disuse atrophy of detrusor muscle of the bladder wall from prolonged anuria. When bladder outlet obstruction is excluded and evaluation reveals the bladder not reparable or usable with acceptable results, BAS with UC could be considered [14].

Adaptation of Inactive Bladder

Urinary retention in the bladder is defined as persistence of urinary retention requiring Intermittent Catheterization (ISC) or Indwelling Urinary Catheter (IUC) for more than 2 months [14]. This period of 2 months is considered as post-transplant adaptation for bladder atonia when other causes of urinary retention is excluded by pre-transplant bladder evaluation for cases that are considered BAS.

Urodynamic Evaluation before Renal Transplant

Who will require urological evaluation pre-transplant?

As transplant patients are continually growing in numbers, and as getting renal donors is increasingly becoming difficult, these together with the consequent prolong waiting time, the state of anuric condition in ESRF patients on dialysis, is also exceeding the limit of 2 years in many situations. As a consequent, the risk of bladder dysfunction from disuse related bladder atrophy pose a risk of subsequent urinary retention post-transplant [14,15]. Along with it the age of the prospective transplant recipients is also increasing posing the risk of developing prostatic hypertrophy in male and Uterovaginal prolapse in female. The likelihood of having an associated cause of neurogenic bladder in case of diabetic neuropathy or residual vesicoureteric reflux in adult needs to be excluded.

Urological evaluation

A plain Ultrasound Scan (US) of urinary bladder and prostate are simple noninvasive investigations that will exclude enlarged prostate and atrophied bladder. Presence of residual urine volume in an anuric patient could be non-significant and merely represents bladder sweet [12,16]. Urodynamic study including voiding cystourogram in pre-transplant state has no role in anuric ESRF patients. However, post-transplant persistent anuria (more than 2 months) would be

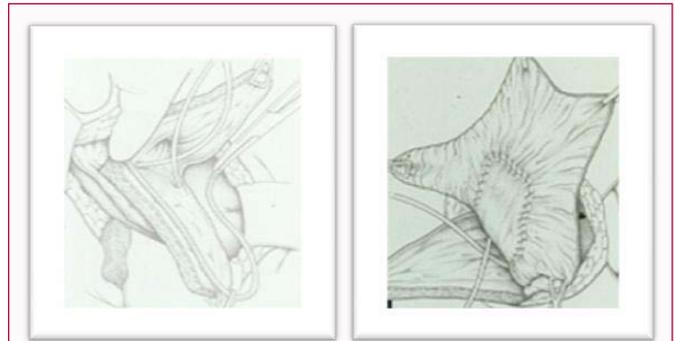


Figure 2: (A) Bivalving of urinary bladder, (B) Stitching of detubularized patch of ileum to the cut bladder.



Figure 3: (A) Megaloureter before ureterocystoplasty, (B) After Ureterocystoplasty.

benefitted to evaluate the bladder action and post-voidal volume. In addition to delineating possible Vesico-Ureteric Reflux (VUR), it confirms degree of bladder atonia and requirement for BAS. In addition, urethroscopy and urethrocytography may contribute to the objective findings of US and urodynamic study [17].

Frequency of BAS in Renal Transplant

In setting of pediatric transplant, where ESRF is commonly related to congenital urological issues, BAS is considered a better option than ileac conduit urinary diversion in transplant recipient [6,7]. In these situations BAS is done before, after or at the time of transplant depending on the individual scenario. The complications related to graft survival and urinary tract infection between each procedure does not differ significantly [18,19]. In adult setting, BAS is only considered when the ESRF was the result of same congenital abnormalities as mentioned above, where the requirement of dialysis occurred in adulthood. In other cases of ESRF from adult origin, the requirement of BAS is less than 0.5% in a large cohort of adult renal transplant [13]. The incidence of BAS in adults is a rarity in transplant literature.

Surgical Techniques

Native dilated ureter is used for BAS as Uretero Cystoplasty (UC) as the native kidneys are nonfunctional rendering native ureter unused, thus making it available when there is ureteromegaly. This procedure is much more acceptable than other alternatives like ileac conduit as that is associated with higher incidence of urinary tract infection and electrolyte and acid-base related metabolic abnormalities [10,20-22]. Therefore urological evaluation before prospective renal transplant recipients requiring BAS is required to

Table 2: Comparative complications of BAS and post-transplant complications, graft function and survival.

Complications	Enterocystoplasty	Ureterocystoplasty	Normal bladder
Episodes of UTI (N=1406 over 20 years)	*23 (N=16)	*6 (N=8)	2 (N+1382)
Graft function (mean \pm SD)	**1.72 \pm 0.31	**1.37 \pm 0.13	1.33 \pm 0.59
Normal graft function	**11	**7	24
Other complications	1. Hyperchloremic acidosis		
	2. Hypokalemic acidosis		
	3. Osteoporosis		
	4. Hematuria-dysuria		
	5. Malignancy risks		
	-Adenocarcinoma		
	-Transitional cell carcinoma		

confirm dilated ureter availability for UC. If the ureter is not dilated UC may not be surgically possible and enterocystoplasty with a segment of small intestine needs to be considered.

BAS technique for enterocystoplasty

In enterocystoplasty, a segment of bowel is used. A detubularized patch of ileum is taken from near ileocecal part and anastomosed with bladder that has been cut in a bivalve fashion to accommodate the bowel segment (Figure 2).

BAS technique for ureterocystoplasty

In ureterocystoplasty, a detubularized part of the dilated ureter is stitched to the bivalved bladder (Figure 3). Dilated ureters are mobilized and opened on their anterolateral surface from 3 cm of Uretero-Vesical Junction (UVJ). The bladder is opened in the midline and bivalved. The medial edges of ureters are then sutured to each other and the lateral edges were sutured to the bivalved bladder halves. Resulting in a dome shaped bladder [23].

Outcome of BAS in Renal Transplant

Graft survival and patient survival

One longitudinal study compared the outcome of EC and UC in renal transplant population over a period of 20 years and compared them with transplant patients with normal bladder. The mean follow up period was 5 years post-transplant (n-1406 with BAS done in 24 patients) [13]. Demographic were identical in the three groups. There was no significant difference in graft survival or patient survival at 1 year. However, 5 year graft and patient survival were non-significantly lower in both EC and UC group as compared to normal bladder group (Table 2).

Infective complications

Pyelonephritis requiring hospitalization of recipients occurred 23 times in EC group and six in UC group. However, 2 patients with normal bladder had Pyelonephritis. These differences were significant between EC and UC group ($p=0.025$) and EC and normal bladder group ($p<0.001$), but not between UC and normal group ($p=0.31$). That indicated that UC, when possible in cases of obstructive uropathy could be better option than EC [13].

Long-Term Complication of BAS in Renal Transplant

Graft related

There were no significant differences among the three study groups in terms of follow-up period, and mean serum creatinine

level [13]. However in pediatric population, long term complications include recurrent urinary tract infections. This is particularly prevalent in cases of non-compliance to the clean intermittent self-catheterization for voiding and or the presence of associated Vesico-Ureteric Reflux [1].

Other long term complications include urinary stones, perforation, need for intermittent self-catheterization and malignancy. These are particularly prevalent in EC rather than UC. Bladder stone has been reported to be around 40% mainly due to stasis of urine in atonic bladder. Increased excretion of calcium in urine, as explained below, also contributes to urinary calculi. Most of the malignancy happened after a prolonged latent period and mostly are adenocarcinoma [24]. Routine cystoscopy has been recommended yearly after a 10 years of BAS [24].

Metabolic systemic complication

As intestinal epithelium is not customized to urine in physiology, metabolic abnormalities with electrolyte and acid-base disorder may complicate the long term morbidity. Hyperchloremic metabolic acidosis can occur as a result of absorption of urinary ammonium with its chloride salt, and secretion of sodium bicarbonate by the intestinal epithelium in EC. This resembles Type 1 Renal Tubular Acidosis (RTA) [25,26].

Chronic acidosis results in osteoporosis because of increased bone resorption. This leads to growth retardation in children and also causes renal stone production because of increased urinary excretion of calcium salts [27].

Long term complications in adults

We reviewed three studies of adult BAS with long-term follow up. The infective complications, requirement of ISC, urinary stone, malignancy and metabolic complications were similar to those of pediatric BAS. The graft function and survival were not affected by BAS [28,2,13].

Current Prospective of BAS in Adult Transplantation

Perspective of nephrologist

While children with congenital urinary abnormalities with ESRF were denied renal transplantation in the past, BAS has made that possible with good graft and patient outcome in the current decade [1]. Extrapolating the success in pediatric population, adults with structural urological abnormalities with ESRF could potentially become candidate for potential renal transplantation with BAS

bringing in the hope [13]. In this perspective, the nephrologists have a role in selection and optimization of the potential transplant recipient, and organizing the urological procedure for BAS either pre-transplant or post-transplant. These include urological studies including CT KUB to delineate the lower urinary tract status, and the urodynamic study to identify the functional integrity and capacity of the urinary bladder. A referral to urologist for these processes could be initiated once the nephrologist is sufficiently confident of the prospect of BAS, and the potential recipient is clearly accepting the procedure and outcome. In adults ESRF, whether due to urological disorders of lower urinary tract initiated in childhood as congenital anomalies or due to lower urinary tract obstruction with megaloureter leading to ESRF, BAS could potentially make renal transplant a viable option that is thought to be a challenge until now.

The issue of bladder atonia from prolonged inactivity of many years from non-functional kidneys in patient on dialysis needs nephrologist's consideration of adaptation period of urinary retention requiring intermittent catheterization or indwelling urinary catheter for 2 months [14]. This period of 2 months is considered as post-transplant adaptation for bladder atonia recovery. In this situation, urological evaluation is needed to exclude other causes of urinary retention before considering BAS.

Perspective of urologist

Urologist and transplant surgeons would be interested in BAS, apparently an uncommon and previously scanty practiced procedure, in adult transplantation. Current practice of transplantation of allograft kidney, does not involve urinary bladder other than implantation of allograft ureter to the bladder in oblique fashion [29]. With the consideration of BAS, perspective of a new urological strategy of evaluation and surgical technique either pre-transplant or post-transplant, as described above, would appear in urologist's domain. A close coordination between urologist and nephrologist, together with the potential transplant recipient, would be needed for elaboration of the need, risk assessment, patients' practice requirements, short term and long term complications in the post-transplant period.

Perspectives of allograft recipient

As mentioned above, the apparent contraindication for transplantation in ESRF due to congenital lower urinary tract abnormalities and neurogenic bladder may be obviated with a renewed prospect of BAS [1]. In addition, newly transplanted patients with prolonged and unresolving bladder atonia post-transplant as explained earlier requiring persistent IDC or ISC, could also become potential candidates for BAS [14]. In this field of prospective BAS, patients need to be educated regarding the need, risk assessment, patients' practice requirements, short term and long-term complications in the post-transplant period. Motivation of patient needs to be assessed by clinical psychologist, and impact of cost to be evaluated by medical social service personnel. Informed consent from the patient and their care givers needs to be documented to avoid future legal mitigations.

Conclusion

BAS in adult renal transplantation, unlike that of pediatric transplantation, would be a change maker procedure for prospective renal transplant recipients for whom transplant would be hitherto remained a contraindication. For recipients with prolonged post-transplant bladder atonia requiring graft-lifelong IDC or ISC, with

risks of recurrent UTI and graft dysfunction, BAS could pose a reasonable remedy. This field would generate interest in the renal transplant community substantially.

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