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Review article

Pre-transplant management of valve bladder: A critical literature review

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Keywords
Posterior urethral valves; Kidney transplant; Augmentation cystoplasty; Valve bladder; Bladder dysfunction

Abbreviations
RT: renal transplantation; PUV: posterior urethral valves; ESRD: end stage renal disease; BD: bladder dysfunction; CIC: clean intermittent catheterization; AC: augmentation cystoplasty; PVR: post-voiding residuals; VB: valve bladder; UDS: urodynamic study; VUR: vesicoureteral reflux; UTI: urinary tract infection; LUTS: lower urinary tract symptoms

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Summary

Objective
Indications, timing and problems related to augmentation cystoplasty (AC), in the context of posterior urethral valves (PUV) and renal transplantation (RT) are ill defined. Associated bladder dysfunction (BD) is not a stable condition and may cause the loss of the renal graft. Polyuria, accentuates BD and seems to improve after RT. The objective of this research is to critically review the available literature, aiming to rationalize the treatment of PUV with BD in the context of end stage renal disease (ESRD).

Materials and methods
A thorough literature review was performed. Pertinent papers were, critically analyzed and classified according to the level of evidence.

Results
Data relating to PUV, RT and AC showed low levels of evidence. Results of RT in PUV cases with adequate management of BD were comparable to those suffering from other causes of ESRD. Bladder function can recover spontaneously after urinary undiversion. There were no established criteria to indicate AC in the context of ESRD and PUV or to define the ideal protocol to treat associated vesicoureteral reflux (VUR). Urinary tract infections (UTIs) were more frequent in transplanted PUV patients; this is possibly related to the inadequate control of BD, especially after AC. AC is feasible after RT with outcomes comparable to preemptive ones.

Conclusion
AC increases the risk of UTI after RT. Preemptive AC should be constructed only if the risks associated with increased bladder pressures exceed those associated with AC. Adequate management of BD is essential to improve bladder function and to minimize UTIs. AC is feasible after RT, with complication rates similar to the ones performed beforehand. Since a considerable number of PUV patients with high-pressure bladders eventually develop myogenic failure, it seems logical to postponing AC in this population, as long as they are under close surveillance.

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Introduction

Bladder dysfunction (BD), polyuria [1] and renal dysplasia are associated with PUV. Bladder dysfunction manifestations in PUV are variable, evolving from high pressure/low compliance in infants to myogenic failure/high capacity bladders in school-aged boys. One third of people with PUV present with severe BD, which should be treated before renal transplantation happens (RT) [2]. Pharmacotherapy, intermittent (CIC) and/or overnight catheterization, augmentation cystoplasty (AC) and diversions are all possible therapeutic alternatives [3,4], but protocols are ill defined and controversial. Augmentation cystoplasty complications include metabolic problems, lithiasis and carcinogenesis [5]. In addition, it implies lifetime CIC, bacteriuria and higher risk of UTI.

Good-quality evidence relating to BD, PUV and RT is scarce. Reports about RT and BD are mostly small, retrospective and descriptive cohorts that are treated for long periods of time, with modifications in RT protocols along the way; PUV cases are often pooled together with other diseases.

The objective of the present study was to critically review the available data, aiming to rationalize the treatment of boys presenting with PUV, BD and terminal kidney failure, waiting for RT.

Methods

A literature review using MEDLINE (PUBMED), Cochrane Library and LILACS databases was conducted with the terms 'POSTERIOR URETHRAL VALVES' AND TRANSPLANT* AND KIDNEY without any limits (strategy 1), and the terms AUGMENTATION AND CYSTOPLASTY AND TRANSPLANT* with age limits (children from 0 to 18 years old) (strategy 2).

The relevant abstracts were reviewed and pertinent papers were critically analyzed. Other articles of interest were acquired from the reference lists. Papers in English, Portuguese, Spanish and French were accepted. Editorials and reviews were excluded.

The degrees of evidence were defined as:

1. Evidence level I: prospective, randomized trial.
2. Evidence level II: prospective, non-randomized, comparative trial.
3. Evidence level III: case control retrospective study.
4. Evidence level IV: descriptive series.
5. Evidence level V: expert opinion.

Results

A total of 186 abstracts were retrieved using the two search strategies. Forty-seven papers met the inclusion criteria and were reviewed *in toto*. Strategy 1: 109 abstracts reviewed, two exclusions because of language restrictions, two reviews excluded, 58 papers not relevant, 41 papers reviewed. Strategy 2: 77 abstracts reviewed, 71 papers not relevant, six papers reviewed. There were no prospective studies among the surveyed papers. All available evidence corresponded to level 3 or 4 quality.

Transplantation and PUV: general information

PUV represents 0.8—16% [6,7] of pediatric RT patients (mean 8.2%); 15—71% (mean 36%) present with low urinary tract symptoms (LUTS) [8,9]. The RT outcomes in PUV are comparable to those in non-urological kidney failure or other urological diseases [1,2,10,11]. Few authors have shown worse results in PUV patients (as compared to primary VUR [9] or 'clinical' cases [12]), but graft losses are attributed to problems unrelated to BD (vascular complications [9] and rejection/non-compliance to immunosuppressive therapy [9,12]). Bartsch et al found worse graft function in a subgroup treated with high diversions, AC (2/10 patients) or urethral complications pre-RT have been detected, suggesting that BD is important to the outcomes (mean clearance 33.8 $\pm$ 9.3 ml/min/1.73 m^2 in the diverted group vs 60.4 $\pm$ 10.8 ml/min/1.73 m^2 in PUV treated with valve ablation/provisional vesicostomy vs 70.2 $\pm$ 21 ml/min/1.73 m^2 in 'clinical' disease cases), but BD management was not clearly described [12]. Fine et al., however, compared valve ablation alone with urinary diversion, and found no differences for bladder behavior at the time of RT. Those treated with valve ablation alone actually had worse results (6/12, 0/7 and 3/12 graft losses in valve ablation, vesicostomy and high diversion groups, respectively). Bladder dysfunction was clearly related to graft loss (56% vs 27% for UD unstable vs stable bladders, OR 3.3), despite no clear description of the treatment strategies that were employed [1]. In Crowe's paper, RT results on 'normal' (mainly VUR) and augmented (4/6 PUV) bladders were clearly better than those on non-augmented 'abnormal bladders' (4/7 graft losses) and ileal conduits. Establishing CIC saved at least two grafts, while non-compliance with CIC led to progressive worsening in three patients [13].

Bladder dynamics, PUV and renal transplantation

Small bladders, secondary to oligoanuria after 'clinical' end stage renal disease (ESRD), recover spontaneously with cycling, turning RT safe [14,15], but VB that aren't functionally or histologically normal may perform differently [16]. Moreover, VB characteristics typically change over time: hypertonic unstable bladders are present in 66% of $<$5 year olds vs 15% of 13-year-old PUV cases. Post-voiding residuals (PVR) tend to increase progressively: at 20 years, two thirds of PUV patients have high PVR [16,17]. Three successful RT into native bladders after resection of augments were reported, reinforcing the idea that VB urodynamic function evolves over time [18]. The natural history of bladder dynamics is also influenced by treatment (drugs, urotherapy and/or CIC) and polyuria.

Herthelius and Oborn have suggested that RT *per se* may modify normal bladder dynamics. These authors evaluated post-RT bladder function on 68/73 pediatric patients, who were subdivided into urological (eight PUV and four prune belly), congenital and acquired 'clinical' ESRD. Although daytime incontinence was present in six out of eight urological patients, abnormal bladder capacity, abnormal flow curves and high PVR were verified in the three groups and were more common than in 'normal' children [10].