Topic 3: Management of children with vesicoureteral reflux and bladder/bowel dysfunction

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The 4-year-old child with vesicoureteral reflux (VUR) and evidence of clinical bladder/bowel dysfunction (BBD) without evidence of an overt neurological cause.

Introduction

Bladder/bowel dysfunction , dysfunctional voiding, dysfunctional elimination syndrome and dysfunctional lower urinary tract symptoms refer to a common but poorly characterized complex of symptoms typically including urinary incontinence, dysuria, urinary tract infections (UTI), urinary frequency, infrequent voiding and constipation. In this Guideline, BBD is used to describe children with abnormal lower urinary tract symptoms of storage and/or emptying which include lower urinary tract conditions such as overactive bladder and urge incontinence, voiding postponement, underactive bladder, and voiding dysfunction, and may also include abnormal bowel patterns including constipation and encopresis. The age of onset varies; while BBD occurs most often in the immediate post-toilet training years, it may be seen prior to and well after toilet training. While the causes are variable and not well defined, the most common pattern is felt to be due to failure of relaxation of the external sphincter and/or pelvic floor muscles leading to high voiding pressures and incomplete bladder emptying. A similar pattern may be the basis for constipation as well. The result of incomplete emptying of the bladder may predispose to the child to UTI. This, in association with high pressure voiding, may be a significant contributory factor to the natural history and health impact of VUR. The association between these entities has not been clearly defined, but several reports have shown a possible link, generally demonstrating that children with BBD have an increased risk of UTI and decreased rate of spontaneous resolution of VUR.

The appropriate approach to the management of the child with VUR and BBD has not been defined, yet the child with this combination of conditions may be at greater risk of renal injury due to infection. The questions to be asked in this context are whether BBD changes the natural history of VUR relative to that of children without BBD and whether the child with BBD is at a higher risk of renal injury or reduced success with medical or surgical management. It is important to recognize that any evidence-based review is inherently limited by the absence of any standardized description or grading system of BBD as well as the lack of uniform validated therapeutic interventions.

Methodology

Literature Search, Data Extraction, and Evidence Combination

A meta-analysis of the existing literature was performed to determine the impact of BBD on VUR in children undergoing nonoperative or surgical management in conjunction with management for elimination symptoms. Outcomes included the resolution of VUR, the incidence of UTI recurrence in children receiving medical management, and open surgical intervention subsequent to medical or endoscopic management, and the incidence of renal cortical scarring. Twelve articles described comparative studies (five were prospective) of VUR in children with or without BBD. Most children diagnosed with VUR by cystography had a previous UTI.

In all, data from 15 articles with 16 arms published between 1997 and 2006 were extracted and meta-analyzed. These reports included 2,039 children with VUR, 75% of whom were female and 640 who had a concurrent diagnosis of BBD. In children with VUR and BBD, 387 received medical management, 114 had endoscopic injection therapy and 139 had open surgery. Of those without BBD, 398 received medical management, 501 had endoscopic injection therapy, and 500

had open surgery. The mean duration of follow-up was 2.5 years for patients receiving continuous antibiotic prophylaxis (CAP) and 1 year for patients treated with endoscopic injection therapy or open surgery.

The treatments for BBD identified in the literature included bladder retraining (timed voiding, relaxed voiding, biofeedback) with or without pharmacologic (anticholinergic) intervention directed at decreasing bladder overactivity, and/or management of constipation (e.g. stool softeners). A wide range of interventions was described and there was no reliable means to compare outcomes by treatment; consequently, the results are considered in the aggregate.

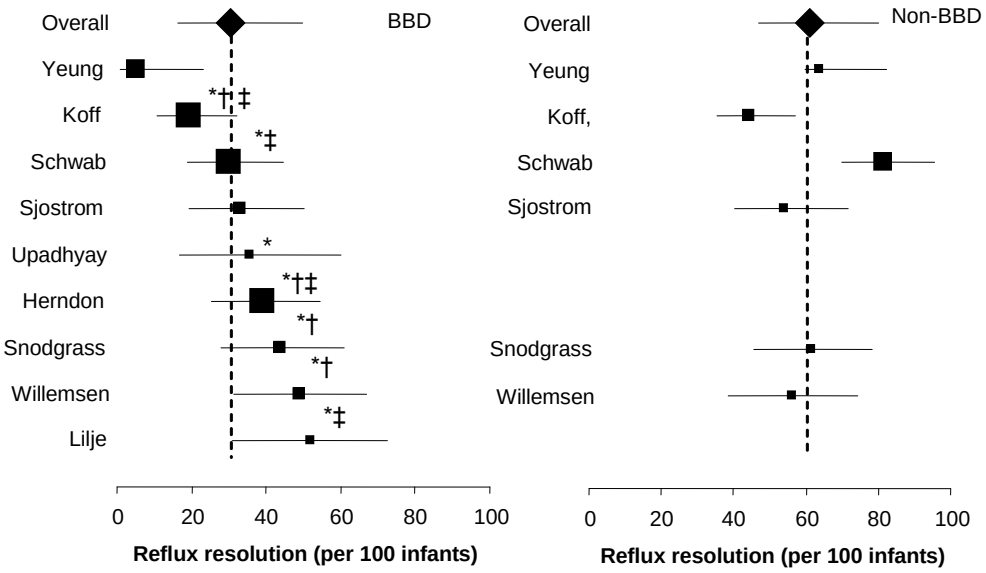
Outcomes Analysis

Vesicoureteral Reflux Resolution

In children receiving CAP, resolution rates were 31% for those with BBD and 61% for those without BBD (Figure 1).

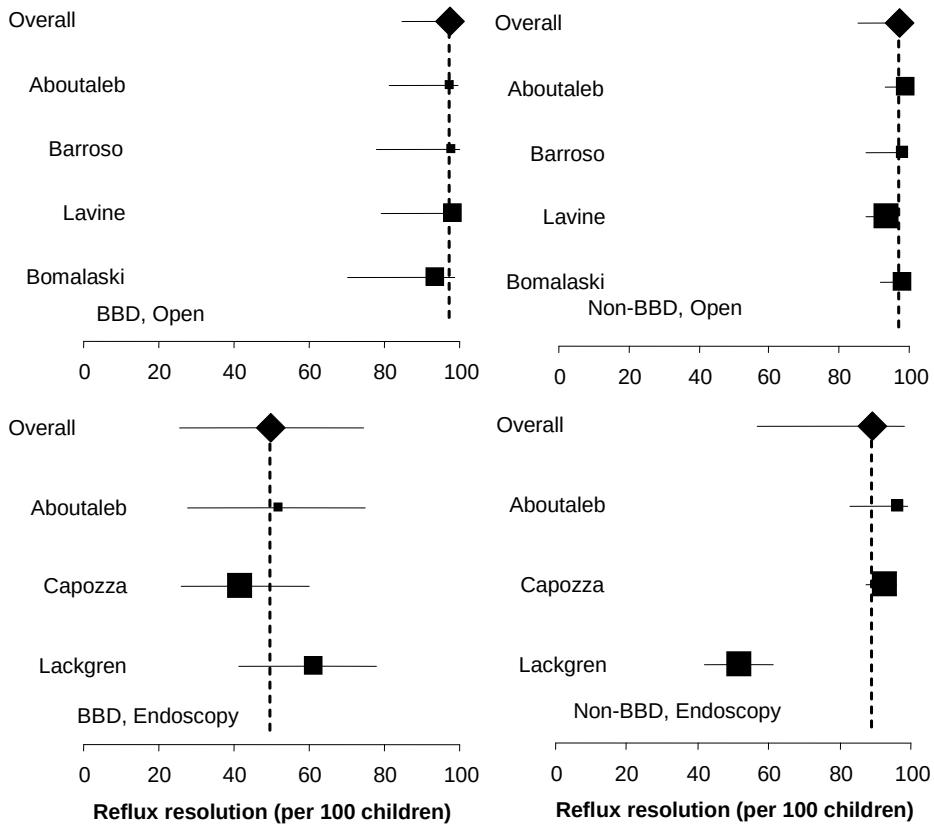
Figure 1. Forest plots of reflux resolution among children receiving continuous antibiotic prophylaxis

(Concurrent/prior use of: *bladder training, †anticholinergics, ‡stool softerners)



In children treated with endoscopic surgery resolution rates at initial follow-up were 50% for those with BBD and 89% for those without BBD (Figure 2) For children treated with open surgery, the presence of BBD did not appear to alter surgical resolution rates, which were 97% in both groups (Figure 2). In each of these groups the specific means of treating BBD and its efficacy cannot be assessed.

Figure 2: Forest plots of reflux resolution in children undergoing intervention with curative intent (open surgery or endoscopic)



Four main criteria were generally used to recommend surgery following CAP or endoscopic surgery: persistent high-grade reflux, breakthrough UTI, treatment noncompliance and/or deterioration of renal function. The time to resolution in those receiving medical management ranged from 3 to 71 months in the BBD group. No data were available regarding the specific treatments for BBD and the time to resolution of VUR. The relationship between VUR grade and time to resolution could not be assessed in either group.

The rate of open surgical correction in children who had previously been receiving CAP was 16.0 (95% confidence interval [CI]: 5.1, 40.3) per 100 cases. In children receiving CAP or undergoing

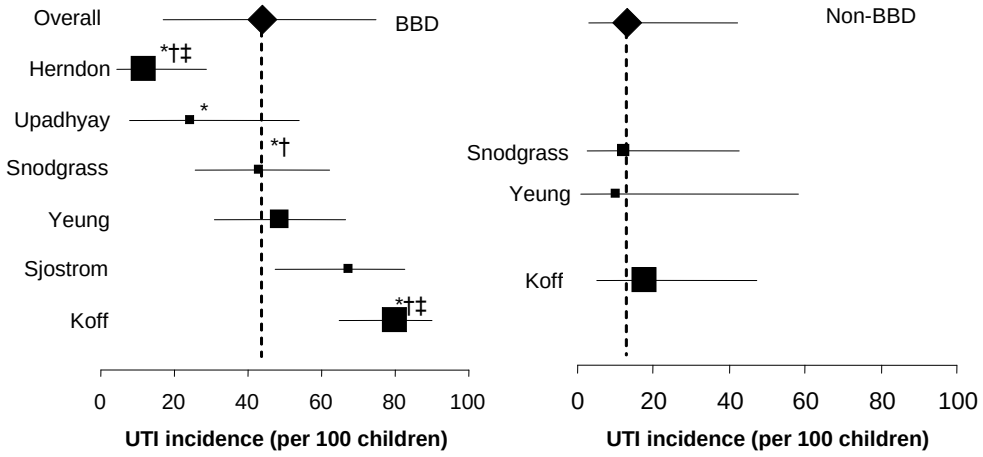
endoscopic therapy, the open surgery rate was 8.3 (95% CI 2.1, 27.6) per 100 cases. Of those children initially receiving CAP, open surgical correction was performed at a mean of 30 months after initiation of CAP. A high risk of recurrent UTI, perhaps based on a history of more frequent UTI's, was the most frequent reason for surgical intervention, followed by lack of resolution with observation.

Incidence of Urinary Tract Infection

Eight studies provided data on the incidence of UTI during follow-up for 918 children with VUR, of whom 374 had concurrent BBD. The incidence of UTI managed with CAP was 44.0% (95% CI: 17.1, 74.9) in children with BBD and 12.9% (95% CI: 2.9, 42.0) in those without BBD. A large variation existed in the overall estimate of UTI in patients with BBD managed medically compared to those without BBD (Figure 3).

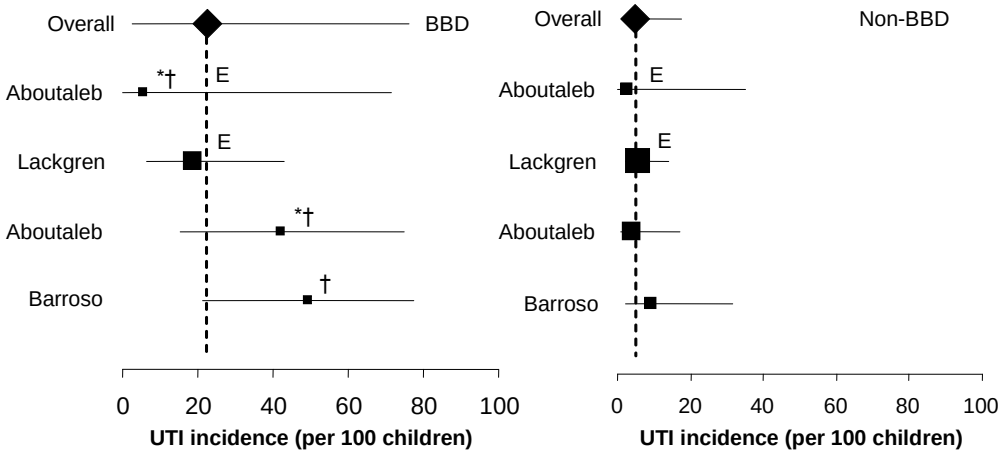
Figure 3. Forest plots of UTI incidence in children receiving medical management (BBD vs. non-BBD)

***bladder training; †anticholinergics; ‡stool softeners**



Following open or endoscopic surgery, the incidence of UTI during follow-up was 22.6% for children with BBD and 4.8% for children without BBD (a nonsignificant difference) (Figure 4). BBD outcomes were not stratified by sex, grade or laterality for the BBD and non-BBD groups. Renal function was not specifically assessed, representing the main limitation of this analysis.

Figure 4. Forest plots of UTI incidence in children following open or endoscopic surgery (BBD vs non-BBD)



*bladder training; †anticholinergics

Renal Cortical Abnormalities

Five studies reported on renal outcomes in children, with two of these studies specific for children with BBD and VUR. Renal cortical abnormalities at baseline ranged from 25% to 30% in those children screened with DMSA (technetium-99m-labeled dimercaptosuccinic acid) scintigraphy. These rates are about twice those found for neonates/infants managed with antibiotics (see Chapter 2) and those in the asymptomatic siblings (see Chapter 4). There were insufficient data to determine the impact of BBD management on the rate of progression of renal scarring or the risk of new renal cortical abnormalities.

Recommendation: Symptoms indicative of bladder/bowel dysfunction should be sought in the initial evaluation, including urinary frequency and urgency, prolonged voiding intervals, daytime wetting, perineal/penile pain, holding maneuvers (posturing to prevent wetting), and constipation/encopresis.

[Based on Panel consensus]

Recommendation: If clinical evidence of bladder/bowel dysfunction is present, treatment of bladder/bowel dysfunction is indicated, preferably before any surgical intervention for VUR is undertaken. There are insufficient data to recommend a specific treatment regimen for bladder/bowel dysfunction, but possible treatment options include behavioral therapy (see Glossary for description), biofeedback (appropriate for children more than age five), anticholinergic medications, alpha blockers, and treatment of constipation. Monitoring the response to bladder/bowel dysfunction treatment is recommended to determine whether treatment should be maintained or modified.

[Based on Panel consensus]

Recommendation: Continuous antibiotic prophylaxis is recommended for the child with bladder/bowel dysfunction and VUR due to the increased risk of urinary tract infection while bladder/bowel dysfunction is present and being treated.

[Based on review of the data and Panel consensus]

Summary

Based on the results of this meta-analysis, children with BBD have a lower spontaneous VUR resolution rate, an increased risk of UTI (both before and after surgical correction), and a lower rate of correction after endoscopic surgery. The success rates of VUR correction with an open approach were equivalent regardless of BBD status. The incidence of baseline renal cortical abnormalities in children with BBD was higher than in infants and young children with VUR but the risk of new renal cortical abnormalites based on BBD status and/or treatment modality of VUR could not be reliably assessed.

Due to the increased rate of UTI associated with BBD, children with VUR should undergo an assessment of voiding and bowel habits. Abnormal voiding patterns should be treated in addition to preventative treatment of UTI. Due to the higher rate of UTI in children with BBD in association with VUR, CAP is recommended at least until the voiding patterns have improved. Correction of BBD should also be undertaken prior to surgical therapy unless clinical conditions are such that intervention is considered imperative, particularly in those with uncontrolled breakthrough UTIs or progressive renal damage. In that setting, open surgical correction appears to have the greatest likelihood of a cure.