Vesicoureteral Reflux: Who Benefits from Correction

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KEYWORDS

• Vesicoureteral reflux • Dimercaptosuccinic acid
• Urinary tract infections • Pyelonephritis

There has been an emergence of a therapeutic nihilistic attitude about the surgical treatment of vesicoureteral reflux (VUR). Evidence-based reviews have questioned whether surgical treatment is beneficial for children with VUR.[1,2] Even the use of prophylactic antibiotics, which have traditionally been the first-line therapy recommended for virtually all patients with VUR, has come under scrutiny after several randomized controlled trials found them to have no effect on decreasing the risk of urinary tract infections (UTIs) in children with VUR.[3–5] This issue is now the primary focus of the current randomized, double-blinded, placebo-controlled trial in children with VUR and UTIs in the United States—the RIVUR trial.[6] This nihilistic pattern challenges the effort that was put forth decades ago to evaluate children with UTIs for anatomic abnormalities, primarily VUR. Now more than ever, urologists treating VUR face a difficult decision process in deciding which patients should be followed conservatively and which should be offered operative correction. Factors influencing this decision include the risk of developing a UTI, and associated risk factors for UTIs such as voiding dysfunction, risk of development of new renal scars, and chance for spontaneous resolution. It is through consideration of these factors for each individual patient that the urologist tries to optimize the selection of patients who will benefit most from operative therapy. This review explores the important questions that guide the determination of who benefits from surgical treatment. The first question to be answered is, what does surgical correction of VUR do for patients?

BENEFITS OF SURGICAL TREATMENT OF VUR

In the 1990s, the first American Urological Association (AUA) panel to develop guidelines for the treatment of VUR was convened, and their summary statement was published in 1997.[7] This meta-analysis of multiple prior treatment options gave recommendations for the treatment of boys and girls with primary VUR from birth through age 10 years. The panel stratified their recommendations based on whether or not renal scarring was present. Surgical treatment was recommended for patients initially older than 1 year with grade V or bilateral grades III and IV if renal scarring was present. No consensus was reached as to what to do at the opposite end of the spectrum, such as those with persistent grades I to II VUR without renal scarring.

Surgical correction of VUR can be accomplished either by ureteral reimplantation or by endoscopically injecting a bulking agent at the ureterovesical junction. The success rates for ureteral reimplantation is routinely reported to be greater than 95% for grades I to IV, with slightly lower success rates for grade V.[8–11] Endoscopic treatment is a less successful but shorter outpatient procedure with minimal morbidity. Published success rates have been reported to be more

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than 90%,[12] but a recent meta-analysis probably gives a more realistic estimate. A single injection is successful for 67% of patients, and with a second injection the aggregate success rate increases to 87% of patients.[13] There is a significantly lower success rate for a third injection (34%); thus, after a second attempt at endoscopic injection, failures should be treated by other means. There is no debate that reflux can be corrected with surgery. More important are the benefits children may receive by no longer having VUR.

Only a few randomized studies compare observation on prophylactic antibiotics with surgical correction.[14–18] The largest study was the International Reflux Study. A summary of randomized studies of surgical correction of VUR is shown in **Table 1**. The main benefit demonstrated in these studies is that children are significantly less likely to develop pyelonephritis after surgical correction of VUR.[1] In the International Reflux Study, the overall rates of UTIs in the medical and surgical arm at 5 years were about 30%.[15] In the United States, the rate of pyelonephritis was 8% for the patients treated surgically versus 21% in those treated medically. In addition, only 10% of the medically treated patients had resolution of VUR at 5 years and only 47% at 10 years, whereas virtually all of the surgically treated patients were free of VUR.[19] Renal growth, the incidence of new renal scars, rates of hypertension, and progression to renal failure do not seem to be altered by surgical treatment.[17,20–22] Although the benefits of surgical correction of VUR have not been what was initially hoped, the surgical treatment of VUR has a low complication rate, high success rate, and has not been harmful to renal function. There has been only one randomized study of patients treated endoscopically, which examined primarily rates of VUR present at 1 year after treatment.[18] In this study, 61 patients were randomized with 40 undergoing endoscopic treatment with dextranomer/hyaluronic acid (Dx/Ha). After 12 months, VUR was present in 62% of the medically treated patients and 31% of the patients treated endoscopically. UTIs were reported in 9 (22%) surgical patients and in none of the patients on prophylaxis; however, the details of the UTIs (pyelonephritis, cystitis, or asymptomatic bacteruria) were not given. A meta-analysis of studies of endoscopic treatment shows a lower incidence of febrile UTIs after treatment.[13] Considering what is known about the benefits of surgical correction of VUR, the focus should be on selecting patients for treatment by identifying those at risk for recurrent pyelonephritis and those in whom VUR will not spontaneously resolve.

URETERAL REIMPLANTATION VERSUS ENDOSCOPIC INJECTION

The controversial topic of whether VUR should be treated with ureteral reimplantation or endoscopic

Table 1
Randomized controlled trials of surgical versus medical therapy for VUR

Study	Description	Summary of Results
Birmingham Reflux Study[14]	Randomized controlled trial (RCT) of severe VUR. Antibiotic prophylaxis vs ureteral reimplantation	No difference in rates of UTI, renal growth, new or progressive scarring after 5 years
International Reflux Study (Europe, United States)[5,16]	RCT of children age <11 y with grade III or IV VUR. Antibiotic prophylaxis vs ureteral reimplantation	No difference in overall rate of UTI or new scar formation at 5 years. Significantly lower rate of pyelonephritis in the surgical group
Smellie et al[17]	RCT of children age 1–12 years with bilateral grades III–V VUR with bilateral scarring. Antibiotic prophylaxis vs ureteral reimplantation	At 4 and 10 years no difference in renal function, rates of hypertension or renal failure, or renal growth in patients treated medically vs ureteral reimplantation
Capozza and Caione[18]	RCT of children age >1 year with grades II–IV VUR. Antibiotic prophylaxis vs endoscopic injection of Dx/Ha	More UTIs in the Dx/Ha-treated group. Reflux was resolved in 69% of the Dx/Ha-treated vs 38% treated with prophylactic antibiotics at 1 y