

Protocol

Periureteral Bulking Agents as a Treatment of Vesicoureteral Reflux

(701102)

Medical Benefit		Effective Date: 10/01/14	Next Review Date: 07/15
Preauthorization	Yes	Review Dates: 09/10, 09/11, 09/12, 09/13, 07/14	

*The following Protocol contains medical necessity criteria that apply for this service. It is applicable to Medicare Advantage products unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. **Preauthorization is required.** Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.*

Description

Vesicoureteral reflux (VUR) is the retrograde flow of urine from the bladder upward toward the kidney and is most commonly seen in children. The primary management strategies have been use of prophylactic antibiotics to reduce urinary tract infections and, for higher grade disease, surgical correction of the underlying reflux. Injection of periureteral bulking agents is proposed as an alternative to surgical intervention.

Background

Treatment of vesicoureteral reflux (VUR) is based on the assumption that VUR predisposes patients to urinary tract infections (UTIs) and renal infection (pyelonephritis) by facilitating the transport of bacteria from the bladder to the upper urinary tract. Pyelonephritis causes renal scarring in as many as 40% of children, and extensive scarring may lead to renal insufficiency and hypertension. The period between first renal scarring from pyelonephritis and the development of hypertension or end-stage renal disease can be 30-40 years. (1)

In most cases, VUR is diagnosed during evaluation of UTIs. Approximately one-third of children with UTIs are found to have VUR. (2) The average age for the onset of UTI is two to three years, corresponding to the age when toilet training occurs. There also appears to be a genetic predisposition to VUR, and siblings may also be examined. The gold standard for diagnosis is voiding cystourography, a procedure that involves catheterization of the bladder. The severity of reflux is described by a grade, typically with the International Reflux Study Group grading system, which grades severity from I (reflux partway up the ureter) to V (massive reflux of urine up the ureter with marked tortuosity and dilation of the ureter and calyces). Determination of VUR grade is not exact, however, due to factors such as bladder pressure, which may vary at the time of measurement. In general, more severe reflux is associated with higher rates of renal injury, and less severe reflux (i.e., grade I and II) is associated with higher rates of spontaneous resolution and treatment success. (3, 4) Other factors found to be associated with the likelihood of spontaneous resolution of VUR and/or renal injury include age, sex, laterality, presence of renal scars, presence of voiding dysfunction, and history of UTI. (1)

Treatment strategies for VUR include bladder training, antibiotic prophylaxis, and surgical modification of the ureter to correct the underlying reflux. VUR is likely to resolve spontaneously over a period of one to five years; lower grades of reflux (i.e., grades I and II) are associated with a higher probability of spontaneous resolution. (3, 4) The decision to administer prophylactic antibiotic treatment includes the consideration of potential adverse effects of long-term antibiotic treatment, which can include allergic reactions and development of treatment-resistant bacteria resulting in breakthrough UTIs.

Open surgical treatment is typically reserved for patients with high-grade reflux (grades III and IV) or as salvage therapy for those who are noncompliant with antibiotic therapy or have breakthrough UTIs while receiving

prophylactic therapy. Surgical management involves lengthening the intramural ureter by modification of the ureterovesical attachment with reimplantation of the ureter. Success rates for open surgery are reported to be greater than 95% and nearly 100% for patients with lower grades of reflux. In recent years, there have been advances in surgical technique, including use of a lower abdominal transverse incision that leaves a smaller scar. Combined with a reduction in the use of ureteral stents and prolonged catheterization; the changes have led to shorter hospital stays and reduced surgery-related morbidity. Moreover, surgeries can now be done on an outpatient basis. Surgery, however, still involves risks associated with anesthesia and potential complications, such as ureteral obstruction, infection, and bleeding. (1) Some centers have reported using laparoscopic antireflux surgery, but this is technically difficult and has not become widespread. Robotic-assisted laparoscopic methods are being developed to overcome some of the technical difficulties. (5)

Treatment of VUR remains controversial. There is a lack of good evidence that VUR actually increases the risk of pyelonephritis and renal scarring, and the long period of time before renal scarring, hypertension, and end-stage renal disease makes these serious conditions difficult to study. Moreover, VUR has a relatively high rate of spontaneous resolution, more than 60% over five years, so many children may not benefit from treatment. (6) An important challenge is to identify the subset of children most likely to benefit from VUR treatment. At present, in the absence of definitive answers on the utility of treating VUR or the best treatment option, antibiotic prophylaxis to prevent recurrent UTIs and surgery to treat the underlying reflux remain accepted management strategies.

The use of bulking agents in the treatment of VUR has been reported for more than 20 years and has been suggested as an alternative to either antibiotic or surgical therapy. Bulking agents can be injected into tissue around the ureteral orifices to minimize reflux. The STING procedure (subureteral transurethral injection) involves the endoscopic injection of a bulking agent into the submucosal bladder wall just below the ureteral opening. In the more recently used modified STING procedure, the needle is placed in the ureteral tunnel, and the bulking agent is injected into the submucosal intraureteral space. When successfully injected, the compound tracks along the length of the detrusor tunnel and establishes a coapted ureteral tunnel. This endoscopic procedure can be performed in an outpatient setting.

A variety of bulking agents have been tested for biocompatibility and absence of migration. Some of the compounds used in clinical studies are collagen (Contigen[®], Zyderm[®], Zyplast[®]), polytetrafluoroethylene paste (Teflon), polydimethylsiloxane (Macroplastique[®]), calcium hydroxyapatite (Coaptite[®]), and dextranomer/hyaluronic acid copolymer (Deflux[®] or Dx/HA).

Regulatory Status

In 2001, Deflux[®] received premarket application (PMA) approval from the U.S. Food and Drug Administration (FDA) for the “treatment of children with vesicoureteral reflux (VUR) grades II-IV.” Contraindications include patients with nonfunctioning kidney(s), active voiding dysfunction, and ongoing urinary tract infection. Duplicated ureters were initially considered a contraindication to Deflux treatment, but this was changed to a precaution in 2007.

Note: Polytetrafluoroethylene may migrate, causing serious adverse events; this agent is not FDA approved. Coaptite[®], Macroplastique[®], and Tegress[®] are categorized by the FDA as “Agent, Bulking, Injectable for Gastro-Urology Use.” Tegress was voluntarily withdrawn from the market by CR Bard as of January 31, 2007.

Related Protocol

Injectable Bulking Agents for the Treatment of Urinary and Fecal Incontinence

Policy (Formerly Corporate Medical Guideline)

Periureteral bulking agents may be considered **medically necessary** as a treatment of vesicoureteral reflux

grades II–IV when medical therapy has failed and surgical intervention is otherwise indicated.

The use of bulking agents as a treatment of vesicoureteral reflux in other clinical situations is considered **investigational**.

Policy Guidelines

The use of bulking agents is contraindicated in patients with non-functioning kidney(s), hutch diverticuli, active voiding dysfunction, and ongoing urinary tract infection.

Bilateral treatment of VUR is typical.

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this Protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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