New Contralateral Vesicoureteral Reflux after Unilateral Ureteral Reimplantation: Predictive Factors and Clinical Outcomes

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Purpose: Although unilateral ureteral reimplantation for vesicoureteral reflux is highly successful, new contralateral reflux will develop postoperatively in some patients. We examined predictors and clinical outcomes of postoperative contralateral vesicoureteral reflux.

Materials and Methods: We reviewed patients who underwent nontapered unilateral reimplantation for primary vesicoureteral reflux graded on a 3-point scale at our institution from January 1990 to December 2002, and identified those with subsequent contralateral vesicoureteral reflux. We analyzed the association of patient/procedure characteristics with incidence, and time to resolution of contralateral reflux and postoperative urinary tract infection. Multivariable models controlled for variables associated with incidence and time to resolution of contralateral reflux.

Results: A total of 395 patients (77.2% female, median age 5.3 years) underwent ureteral reimplantation for vesicoureteral reflux. Preoperative reflux was grade 1 in 2.8% of patients, grade 2 in 56.6% and grade 3 in 40.6%. Technical success was 95.4%. After reimplantation 39 patients (9.9%) had new contralateral reflux (grade 1 in 7, grade 2 in 27 and grade 3 in 5). Median followup was 51.8 months. On multivariate analysis younger age (less than 6 years, OR 3.7, $p = 0.006$) and low observed bladder capacity as percent of predicted bladder capacity (less than 50% of predicted capacity, OR 6.3, $p = 0.02$) were significant predictors of contralateral reflux. Contralateral reflux resolved in 21 of 27 patients (77.8%) on subsequent cystography at a median of 21.5 months. Two patients underwent reimplantation for persistent contralateral reflux. Four of 39 patients (10.3%) with contralateral reflux had postoperative febrile urinary tract infections at a median of 26 months, with spontaneous resolution of contralateral reflux in all.

Conclusions: Younger patients and those with low observed vs predicted bladder capacity may be at increased risk for postoperative contralateral vesicoureteral reflux. A majority of contralateral reflux will resolve spontaneously, and the clinical course is typically benign.

Key Words: vesico-ureteral reflux; surgical procedures, operative; follow-up studies

Abbreviations and Acronyms

BC = bladder capacity
C-VUR = contralateral vesicoureteral reflux
IRS = International Reflux Study
RNC = radionuclide cystogram
UTI = urinary tract infection
VCUG = voiding cystourethrogram
VUR = vesicoureteral reflux

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ALTHOUGH unilateral ureteral reimplantation for vesicoureteral reflux is highly successful, a small percentage of patients experience de novo contralateral vesicoureteral reflux postoperatively.[1–5] There are few data

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regarding risk factors for contralateral reflux, and its clinical significance is uncertain. Given the high success rate of bilateral reimplantation, one option is to reimplant both ureters in all patients with unilateral reflux. However, a less aggressive strategy may be to identify preoperative risk factors for contralateral reflux in patients with unilateral reflux and to perform selective bilateral reimplantation. We sought to examine predictors and clinical outcomes of postoperative contralateral vesicoureteral reflux.

METHODS

With institutional review board approval, we performed a retrospective billing and medical record review of all patients who underwent ureteral reimplantation at our institution between January 1990 and December 2002. We excluded all patients with secondary VUR (due to neurogenic bladder, posterior urethral valves, bladder exstrophy, renal transplant, prune belly syndrome or ureterocele), as well as those who had undergone repeat, laparoscopic or endoscopic procedures and those requiring ureteral tapering.

Surgical outcomes were analyzed for patients with a routine postoperative screening cystogram (RNC or VCUG) performed within 9 months of reimplantation (range 0.9 to 8.9). Patients were excluded if they 1) had no postoperative cystogram available or 2) had undergone initial postoperative cystography more than 9 months after reimplantation. (Late cystography is more likely performed for clinical indications, eg UTI, and may represent a biased sample.) Surgical success was defined as absence of VUR (grade 0) into the reimplanted ureter(s) on initial postoperative screening cystogram, while any degree of VUR (grade 1 or higher) into the contralateral ureter was defined as C-VUR. We evaluated patient and procedure characteristics, and clinical outcomes (VUR, UTI and additional surgery).

Observed bladder capacity was determined by bladder capacity measured on final preoperative cystogram (RNC or VCUG). Predicted bladder capacity was calculated based on the formula proposed by Kaefer et al.[6] Correlation between final preoperative observed bladder capacity (as percent of predicted capacity) and initial postoperative observed bladder capacity (as percent of predicted capacity) was determined using Spearman rank correlation coefficient.

Preoperative VUR was graded based on the final preoperative cystogram. Since most of these cystograms were RNCs, we elected to use the 3-point RNC scale to grade preoperative and postoperative VUR.[7] In cases where the final cystogram was VCUG (typically graded using the 5-point scale based on the International Reflux Study), we converted these scores to the 3-point RNC scale as follows. IRS grade I was converted to RNC grade 1, IRS grade II or III to RNC grade 2 and IRS grade IV or V to RNC grade 3.[8]

In patients with C-VUR the primary outcome was spontaneous resolution of reflux. Resolution was defined as grade 0 VUR on subsequent postoperative cystography following the initial postoperative cystogram. The decision to perform subsequent postoperative cystography was at the discretion of the attending urologist. Because grade 1 VUR is of uncertain clinical significance, we also performed a secondary analysis considering time to resolution of clinically significant (grade 2 to 3) C-VUR. In this analysis resolution was defined as C-VUR grade 0 or 1 on subsequent cystography. Other clinical end points included additional antireflux surgery and febrile UTI during followup. Febrile UTI was defined as temperature of at least 38.5C and/or flank pain and/or acute phase renal scintigraphy documenting evidence of acute infection. Number of colony-forming units required for diagnosis of a UTI was 50,000 or greater for catheterized specimens and 100,000 or greater for clean catch voided specimens.

Bivariate tests of association were performed using Fisher exact test or Wilcoxon rank sum test. Predictive factors of C-VUR were analyzed using multivariate logistic regression. Covariates with a p value of less than 0.2 on bivariate analysis were entered into the initial multivariable model. A backward selection technique was used to identify and remove nonsignificant variables ($p \geq 0.05$). We also performed a survival analysis of time to resolution of C-VUR using Cox proportional hazards regression among patients with C-VUR and more than 1 postoperative cystogram. Patients who underwent additional antireflux procedures on the side of the contralateral ureter were censored in the survival analysis at additional surgery. All analyses were performed using SAS®, version 9.2. Graphs were created using R, version 2.15.2. All tests were 2-sided and $p \leq 0.05$ was considered significant.

RESULTS

Sample Characteristics

We identified 1,413 patients who underwent open reimplantation (unilateral or bilateral) for VUR during the study period, of whom 482 (34.1%) had primary unilateral VUR. Of these patients 445 (92.3%) underwent nontapered unilateral reimplantation. A total of 395 patients (88.8%) underwent postoperative screening cystogram within 9 months of reimplantation and represented the primary analytic cohort. There was a history of C-VUR that resolved preoperatively in 20 patients (5.1%). Patient and procedure characteristics are presented in table 1.

Because some patients did not undergo routine screening cystography within 9 months of reimplantation, we compared these patients with individuals who underwent screening cystography. Patients who underwent postoperative screening cystography were likelier to be younger (median age 5.3 vs 7.9 years, $p = 0.01$), female (77.2% vs 50.0%, $p < 0.001$), and white (89.5% vs 66.7%, $p < 0.002$), to have preoperative grade 3 VUR (40.6% vs 24.0%, $p = 0.03$) and to present with UTI (83.8% vs 68.0%, $p = 0.01$) compared to those who did not undergo