Is Availability of Endoscopy Changing Initial Management of Vesicoureteral Reflux?

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Abbreviations and Acronyms

ARS = antireflux surgery
Dx/HA = dextranomer/hyaluronic acid
EARS = endoscopic antireflux surgery
NC = nuclear cystogram
OARS = open antireflux surgery
PTFE = polytetrafluoroethylene
UTI = urinary tract infection
VCUG = voiding cystourethrogram
VUR = vesicoureteral reflux

Purpose: The optimal management of vesicoureteral reflux continues to be controversial. Since dextranomer/hyaluronic acid copolymer implants were approved in 2001 for endoscopic antireflux surgery, the perception that endoscopy is less morbid than open surgery, combined with concerns over potential adverse effects of prophylactic antibiotics, has led some to advocate endoscopy as initial therapy for reflux. We examined whether the availability of endoscopy has changed the management of reflux.

Materials and Methods: The i3 Innovus database (Ingenix, Eden Prairie, Minnesota) contains longitudinal claims data on more than 39 million patients spanning a 5-year period. We analyzed children diagnosed with vesicoureteral reflux (ICD-9 code 593.7, plus claim for radiographic or nuclear cystogram within 90 days) and at least 1 year of followup. We assessed patient characteristics, and diagnostic and therapeutic interventions. We evaluated surgical trends, including the changing use of endoscopic vs open antireflux surgery.

Results: Among 9,496 children meeting inclusion criteria 1,998 (21%) underwent antireflux surgery during the study period (2002 to 2006). Median followup for surgical cases was 894 days. Of patients undergoing antireflux surgery 1,046 (52.4%) underwent an open procedure and 952 (47.6%) underwent endoscopy. Females were more likely to undergo endoscopy (52% vs 33% of males, \( p < 0.0001 \)), as were children older than 5 years (53% vs 45% of those younger, \( p = 0.0002 \)). Of patients undergoing surgery 1,234 (62%) were treated early (within 12 months of diagnosis). During the study period the rate of newly diagnosed reflux cases managed by early surgery increased from 12.0% to 17.3% (Mantel-Haenszel chi-square test \( p < 0.0001 \)). This increase was primarily due to a more than doubling of patients undergoing early endoscopy (4.2% in 2002 vs 9.7% in 2006, \( p < 0.0001 \)). The rate of newly diagnosed cases managed by early open surgery did not change significantly (\( p = 0.3446 \)).

Conclusions: During a 5-year period after dextranomer/hyaluronic acid was introduced for endoscopic therapy the number of children newly diagnosed with vesicoureteral reflux treated with early antireflux surgery increased significantly due to increased use of endoscopy. This finding suggests that despite the lack of evidence of benefit, endoscopy is increasingly viewed as first line therapy for reflux.

Key Words: economics, medical; endoscopy; urologic surgical procedures; vesico-ureteral reflux
The optimal management of vesicoureteral reflux continues to be controversial. Since dextranomer/hyaluronic acid copolymer was introduced in 2001 for endoscopic antireflux surgery, the perception that endoscopy is less morbid than open surgery, combined with concerns over potential adverse effects of prophylactic antibiotics, has led some to advocate endoscopy as initial therapy for reflux. While many physicians have incorporated endoscopy into their treatment armamentarium, there is little evidence regarding its impact on reflux management and decision making.

We hypothesized that physician perceptions regarding the efficacy of EARS have led to its increased use as primary therapy for VUR compared to traditional antibiotic prophylaxis. We used a large database to investigate patterns of care for VUR with specific focus on trends in use of open vs endoscopic surgery during the period when endoscopy was becoming widely available.

METHODS
We analyzed medical insurance claims data from the i3 Innovus database, which contains data for more than 39 million lives derived from the UnitedHealthcare family of health insurance plans and products. UnitedHealth Group operates in all 50 states, although we do not have information regarding the specific geographic distribution of patients in the database. Although de-identified, the database allows longitudinal followup of individuals during the data period. Information accessible via the database includes diagnoses (via ICD-9 codes), procedures and diagnostic studies including radiology and laboratory tests (via CPT codes), and pharmacy prescribing information including agent(s), dose, duration, and refills ordered and fulfilled. We had access to data from 2002 through the first quarter of 2007. The data were housed at the University of California, Los Angeles and analyzed at RAND.

Included Subjects
Patients were included as subjects if 1) they were 18 years old or younger at diagnosis, 2) ICD-9 diagnosis codes for VUR (593.7, 593.70, 593.71, 593.72, 593.73) were present, 3) CPT codes for radiological diagnostic studies (VCUG, 74455; NC, 78740) were present and 4) at least 1 year of followup after VUR diagnosis was available. To limit the study set to patients with primary VUR, we excluded those with codes for ureterocoele and ureteral obstruction (753.2), neurogenic bladder and spina bifida (596.5, 741), posterior urethral valves (753.6), bladder exstrophy (753.5), renal transplant (V42) and prune belly (756.71). Patients with codes for ureterocele and ureteral obstruction were female and had a urinary tract infection. Radiographic VCUG was the most commonly used initial diagnostic test, and most patients underwent upper tract imaging within 90 days of diagnosis.

RESULTS
Initial analysis of claims data revealed 26,155 patients with a diagnosis code for VUR, of whom 22,862 (87.4%) were children. After excluding patients with no cystographic imaging available (6,989), followup less than 1 year after diagnosis (6,355) and secondary VUR (22) 9,496 records were available for followup analysis. Only patients diagnosed during the first quarter of 2006 were included due to the time limits of the available data and our 1-year followup requirement. Therefore, the number of subjects from 2006 is less than for other study years.

Patient characteristics are outlined in table 1. As expected, most patients were younger than 5 years, were female and had a urinary tract infection. Radiographic VCUG was the most commonly used initial diagnostic test, and most patients underwent upper tract imaging within 90 days of diagnosis.
Median followup was 894 days in the surgical group and 794 days in the nonsurgical group.

A total of 1,998 patients (21%) underwent ARS during the study period, of whom 1,037 (51.9%) underwent OARS and 961 (48.1%) underwent EARS. Differences between the surgical groups are outlined in table 2. Females undergoing ARS were significantly more likely to undergo EARS (p < 0.0001), as were older children (p < 0.0001). Mean time from diagnosis to ARS was longer in the EARS group (p = 0.0035), and patients with a history of UTI were less likely to undergo ARS (18.5% vs 27.7% without UTI, p < 0.0001).

Of patients undergoing ARS 1,234 (61.8%) underwent early surgery (within 12 months of VUR diagnosis). Among the early ARS groups mean time from diagnosis to surgery was 128 days (median 101) for OARS and 129 days (107) for EARS. The OARS group was slightly more likely to undergo early surgery than the EARS group (64% vs 59%, p = 0.03).

When we examined the number of newly diagnosed VUR cases managed by early ARS as a function of year of diagnosis we found that the number increased during the study period (table 3). The increase was primarily due to a more than doubling of the rate of patients undergoing early EARS during this time (see figure). In contrast, the proportion of newly diagnosed cases managed by early OARS did not change significantly during the study period (p = 0.3446).

**DISCUSSION**

Urologists have long sought a less invasive way to correct VUR. The first injection technique was reported by Matouschek in 1981. Using PTFE paste as a bulking agent, he elongated the intramural tunnel and created a more substantial backing for the ureter by injecting PTFE into the submucosa.
may impact practice patterns among urologists treating children with VUR.

Our findings suggest that the trend of early surgery as initial therapy for newly diagnosed VUR may be increasing. Our data span the time frame immediately following approval of Dx/HA for VUR management. Supporters of EARS have aggressively promoted this therapeutic option through the literature. Current standards of care do not yet embrace such early treatment. The current Campbell-Walsh textbook states that “the indications for correction of reflux should remain unchanged regardless of whether reflux is corrected by open surgery, endoscopy, or laparoscopy.”15 However, our data suggest that practice trends may already be leaving the textbooks behind.

This study is among the first to document trends in management of VUR in the community. Most of the urological literature consists of case series from tertiary pediatric care centers, where treatment trends might not reflect actual community standards and practices. One exception is a report by Lendvay et al, who used the Pediatric Health Information System database to analyze trends in VUR surgery.6 However, this data set is limited to highly subspecialized pediatric hospitals and might not reflect broader care in the community or even at all pediatric hospitals. Our results, while qualitatively similar to those of Lendvay et al,6 expand on their findings using a much larger database with a broader subject population. Thus, our findings reinforce and strengthen their observations, giving credence to the notion that a shift in practice patterns is under way.

Generally the effects of new technology and therapies on practice patterns and quality of care have been poorly understood. There have been efforts to document the impact of novel therapies in areas such as cardiology (effects of drug eluting stents on management of coronary artery disease),16 vascular medicine (effects of endovascular procedures on management of abdominal aortic aneurysm)17 and even urology (role of robotic assisted laparoscopy training in surgical practice).18 However, the majority of such studies are limited to single centers or regions, and few seek to create the kind of comprehensive picture of national practice patterns or use longitudinal patient data, as we have done in this study. To our knowledge no such data exist regarding UTI/VUR management trends.

Our finding that 21% of VUR cases were managed by surgery during the study period (with 13% of newly diagnosed cases managed by early surgery) is consistent with some, but not all, previous findings. Among patients in the International Reflux Study 24 of 72 North Americans (33%) were randomized to medical therapy, while only 8 of 155 Europeans (5%)
crossed over to ARS.\textsuperscript{19,20} Arant reported on a longitudinal cohort of 113 patients with primarily grades I to III VUR, of whom only 3 (2.7\%) underwent ARS during the study.\textsuperscript{21} Thus, it appears that contemporary surgical treatment rates for VUR may be higher than those seen historically. The availability of endoscopic ARS as a widely accepted modality may be pushing surgical intervention to the forefront earlier and more aggressively than before. Another factor may be increasing concern over the efficacy (or lack thereof) of prophylactic antibiotics. An additional factor, although difficult to quantify, is the aggressive marketing of endoscopy for VUR to clinicians and the lay public. Marketing can influence physician decision making,\textsuperscript{22} as well as that of families,\textsuperscript{23} who may arrive at the office requesting endoscopic therapy.

Certain limitations inherent in studies of this type need to be considered. First, there are the limitations of using large administrative databases. This database was composed of insurance claims data. Treatment for which no claim was made will not be captured by the database. Conversely we cannot be certain that the appearance of a new claim for a particular diagnostic code reflects the actual timing of the clinical diagnosis. Thus, it is possible that some of our newly diagnosed cases actually were late in the course of the disease. However, we investigated this issue by assessing how many of our newly diagnosed VUR cases had claims data available for more than 6 months before the initial diagnosis. More than two-thirds of the patients had 6 months of data or more (without any VUR related claims), suggesting that a substantial majority of the VUR diagnoses were verifiably new. For the minority without 6 months of prior data there will remain some uncertainty about timing.

In addition, our diagnosis and procedure classifications rely on the ICD-9 and CPT coding systems, and represent secondary data extracted from the original medical record. Therefore, they are subject to potentially inaccurate data transfer or inaccurate coding. Furthermore, these coding systems do not provide us with VUR grade or indications for surgery, which are potentially important covariates. A further limitation is that in using a database of private insurance claims this study, by definition, is restricted to children with private insurance coverage. These patients may differ systematically from those without insurance or with public insurance (eg Medicaid). Thus, the generalizability of these findings is limited.

Finally followup is limited in this context. Although we restricted the analysis to patients with a minimum of 1 year of followup, it is possible that this group differs systematically from those who dropped out of the database before 1 year.

From a practical standpoint these limitations mean that caution should be exercised in generalizing our findings to broader populations. Most specifically these data may not be applicable to uninsured pediatric populations or to those with public insurance such as Medicaid. In these groups VUR management trends may differ due to financial and other pressures affecting families and clinicians. Further work with data that include these populations is needed to extend these results to the broader pediatric population.

**CONCLUSIONS**

During a 5-year period after the introduction of Dx/HA for endoscopic therapy the number of children newly diagnosed with VUR who underwent early ARS increased, primarily due to increased use of endoscopy. This finding suggests that despite the lack of evidence of benefit, EARS is increasingly viewed as first line therapy for VUR.

**REFERENCES**


EDITORIAL COMMENT

The authors raise appropriate concerns as they present evidence of a growing trend toward early endoscopic injection in a large, privately insured North American pediatric population. Regardless of the well acknowledged limitations, this report provides a glimpse at treatment patterns in the United States following approval of Dx/HA. Although the generalizability of the findings is limited, it is unlikely that they represent an isolated phenomenon.

As time goes by, management of VUR seems less well-defined. Paradigm shifts in the surgical arena along with emerging data questioning the benefit of antibiotic prophylaxis make it challenging to counsel families overloaded with conflicting information and concerned about long-term consequences. With such uncertainty it is interesting to see how endoscopic injection has gained such wide acceptance, being embraced by parents, health care providers and third party payers. Many issues that deserve further attention come to mind, such as the potential consequences of increasing late failures.

Just as the Randomized Intervention for Children With Vescoureteral Reflux study has pooled forces to answer important questions, we should strive for higher levels of evidence to help us clarify our approach to this common condition. The perennial plea for well designed trials surfaces yet again. We must take advantage of the momentum and seize the opportunity to define better the role of endoscopic injection for reflux correction.

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REFERENCES

