Surgical Treatment of Vesicoureteral Reflux in Children

Ahmad A. Elderwy, MD
Assistant Professor of Urology
AUNH, Egypt

Feb 4, 2015
Vesicoureteral Reflux

- The Problem of VUR
- Prevention of Surgery
- Surgery or endoscopy
- Optimization of VUR surgery
Vesicoureteral Reflux (VUR)
Principles of Management

1. Spontaneous resolution of reflux is very common.

2. High-grade reflux is less likely to resolve spontaneously.

3. Sterile reflux is benign.

4. Extended use of prophylactic antibiotics is benign.

5. Success of (open) surgical correction is very high.

(Dr. Safwat)
VUR

- **Incidence?**
  - Overall - 1-3%
  - Kids with UTIs - 20-70% (? 20-30%)
  - Kids with fUTIs – 40-50%
  - Siblings: up to 30%

- **Age relationship (pts with UTIs)**
  - <1 yr 70% have VUR
  - 4 yrs 25%
  - 12 yrs 15%
  - Adults 5%
Potential Harms and Costs

- VCUG

- Diagnosis of VUR and perceived risk of renal scarring causes anxiety to patient and family.

- Harms/Costs of treatment potentially great.
Natural history

- **Good news (GI-III)** - spontaneous resolution!
  
  20%/ year

- **Bad news (GIV-V)** - 79% of children with renal scarring
Reflux

- mechanism
  - ‘tunnel’ of ureter into bladder
  - spectrum of pathology + ? Anatomical defects

reflux

Ectopic Normal

neurogenic bladder
valves
Voiding Dysfunction
Prenatal VUR: ? Anatomical
Postnatal VUR: ? Functional
2ry VUR
VUR: Diagnosis

WHO is evaluated?

- Children < 5 years old with UTI (? 2)
- All boys < 10 years old with UTI (? 2)
- Siblings of Refluxers

- Antenatal hydronephrosis confirmed after delivery (? GIII-IV)
International Classification of VUR

VUR: Embryology

Normal ureteric bud induction of the Mesonephros

- Bladder neck, proximal urethra
- Trigone
- Waldeyer's Sheath

Normal development if everything goes right!

Orthotopic, high potential for normal kidney

Dr. Mitchell
Consequences of VUR

- Recurrent Urinary Tract Infection / Pyelonephritis
- Renal Scarring / Reflux Nephropathy
- Hypertension
  - VUR/RN most common cause of HTN in children
  - occurs in 10% cases with scarring
- ESRD (<0.1%)
  - Estimates vary from 5-12% of all ESRD attributable to VUR
Immaturity

UTI

Pre-existing damage

Bladder Dynamics

Renal Injury

VUR

Immaturity

UTI

Pre-existing damage

Bladder Dynamics

Renal Injury

VUR
What patient factors predict high risk for future febrile UTI and scar?

- Age < 1 year
- White race
- High-grade VUR (grades 4 and 5)
- Presence of a renal scar/defect
- Bowel and bladder dysfunction
What is the prevalence of renal scar based on number of fUTIs?

<table>
<thead>
<tr>
<th>fUTIs:</th>
<th>%scars</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5%</td>
</tr>
<tr>
<td>2</td>
<td>10%</td>
</tr>
<tr>
<td>3</td>
<td>18%</td>
</tr>
<tr>
<td>4</td>
<td>33%</td>
</tr>
<tr>
<td>5</td>
<td>62%</td>
</tr>
</tbody>
</table>
Treatment of Vesicoureteral Reflux

- Medical Therapies
  - Antibiotic Prophylaxis + Surveillance
  - Bladder Training

- Surgical Therapies
  - Ureteral Reimplantation
  - Subureteric Injection of Bulking Agents
Treatment of Vesicoureteral Reflux

- Prophylactic antibiotic spontaneous resolution rates
  - 10-25% per year

- Single injection success rates
  - 69-91%

- Open surgical reimplantation success rates
  - 95-99%
What is the Best Treatment of Reflux?

- **VCUG** – how often if at all?
- **Antibiotics** – how long?
- **Surgery** – when?
- **Injection Rx** - when and in whom?
Vesicoureteral Reflux

- The Problem of VUR
- Prevention of Surgery
- Surgery or endoscopy
- Optimization of VUR surgery
Natural History

Spontaneous Resolution of VUR

RD = Renal Disease
DV = Dysfunctional Voiding

Spontaneous Resolution of VUR


Fig. 5. Resolution rate by gender and worst reflux grade.
Is antibiotic prophylaxis useful?
Effectiveness of Interventions for VUR

Open surgical correction of VUR plus prophylactic antibiotics v. prophylactic antibiotics alone to prevent recurrent UTIs

<table>
<thead>
<tr>
<th>Author, Journal, Year</th>
<th>RR recurrent UTI 2 years</th>
<th>RR recurrent UTI 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheeler, ADC, 2003 (meta-analysis)</td>
<td>1.1 (0.6-2.1)</td>
<td>0.99 (0.8-1.3)</td>
</tr>
</tbody>
</table>

Successful Surgery Do prevent febrile UTIs
# Effectiveness of Interventions for VUR

## Outcomes of Medical and Surgical Therapy for Children with Primary Vesicoureteral Reflux and Renal Scarring

<table>
<thead>
<tr>
<th>Registrant</th>
<th>No. of Patients</th>
<th>New Scars</th>
<th>Thinning</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Europe</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical</td>
<td>155</td>
<td>19 (12%)</td>
<td>11 (7%)</td>
</tr>
<tr>
<td>Surgical</td>
<td>151</td>
<td>20 (13%)</td>
<td>15 (10%)</td>
</tr>
<tr>
<td><strong>United States</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical</td>
<td>66</td>
<td>14 (20%)</td>
<td>9 (13%)</td>
</tr>
<tr>
<td>Surgical</td>
<td>64</td>
<td>16 (25%)</td>
<td>2 (3%)</td>
</tr>
</tbody>
</table>
Medical versus surgical treatment in children with severe bilateral vesicoureteric reflux and bilateral nephropathy: a randomised trial.

Smellie JM¹, Barratt TM, Chantler C, Gordon I, Prescod NP, Ransley PG, Woolf AS.

Abstract

BACKGROUND: Nephropathy associated with vesicoureteric reflux (VUR) and urinary tract infection can result in end-stage renal failure, hypertension, or both. Whether long-term VUR contributes to these outcomes is unknown. We compared, in a randomised trial, medical with surgical management of children with bilateral severe VUR and bilateral nephropathy.

METHODS: We stratified by age and glomerular filtration rate (GFR) 25 boys and 27 girls aged 1-12 years and randomly assigned them to medical or surgical management. At enrolment and 4 years' follow-up we estimated GFR from the plasma clearance of 51Cr-labelled edetic acid (EDTA), and did intravenous urography. We also did a metastable 99mTc-labelled dimercaptosuccinic acid (DMSA) assay and contrast cystography. The change in GFR at 4 years, expressed as a percentage change between enrolment and 4 years, was available for 26 of 27 patients in the medical and 24 of 25 in the surgical group. We assessed GFR in 48 patients 10 years after enrolment.

FINDINGS: Mean GFR at enrolment was 72.4 mL/min per 1.73 m² (SD 24.1) in the medical and 71.7 mL/min per 1.73 m² (SD 31.9) in the surgical group. The mean percentage change in GFR at 4 years was 2.4% (SE 4.5) versus 4.7% (SD 5.0) in the medical and surgical groups, respectively. The difference in change in GFR at 4 years between the two groups was not significant (7.1%, 95% CI 6.4% to 20.6%).

INTERPRETATION: Our data do not lend support to the view that the outcome for renal function is improved by surgical correction of VUR in children with bilateral disease.
Swedish Reflux Trial

Prophylaxis n=69

Endoscopic Rx n=66

Surveillance n=68

2 years Follow-up
VCUG DMSA Bladder function

UTI=194
PNH=9
203
128 girls
75 boys
GIII-IV VUR

GIII-IV VUR
The Swedish reflux trial in children: II. Vesicoureteral reflux outcome.

Holmdahl G1, Brandström P, Läckgren G, Sillén U, Stokland E, Jodal U, Hansson S.

Abstract

PURPOSE: We compared reflux status in children with dilating vesicoureteral reflux treated in 3 groups, including low dose antibiotic prophylaxis, endoscopic therapy and a surveillance group on antibiotic treatment only for febrile urinary tract infection.

MATERIALS AND METHODS: A total of 203 children 1 to younger than 2 years with grade III-IV reflux were recruited into this open, randomized, controlled trial. Endoscopic treatment was done with dextranomer/hyaluronic acid copolymer. The main end point was reflux status after 2 years. Data were analyzed by the intent to treat principle.

RESULTS: Reflux status improved in all 3 treatment arms. Of patients in the prophylaxis, endoscopic and surveillance groups 39%, 71% and 47%, respectively, had reflux resolution or downgrading to grade I-II after 2 years. This was significantly more common in the endoscopic than in the prophylaxis and surveillance groups (p = 0.0002 and 0.0030, respectively). After 1 or 2 injections 86% of patients in the endoscopic group had no or grade I-II reflux but recurrent dilating reflux was seen in 20% after 2 years.

CONCLUSIONS: Endoscopic treatment resulted in dilating reflux resolution or downgrading in most treated children. After 2 years endoscopic treatment results were significantly better than the spontaneous resolution rate or downgrading in the prophylaxis and surveillance groups. However, of concern is the common reappearance of dilating reflux after 2 years.
Girls

Logrank p < 0.0001

Probability of no UTI recurrence

Time to first febrile recurrence (months)

1: Endoscopic  2: Prophylaxis  3: Surveillance
Swedish Reflux Study: New Renal Scarring at 2 years

Number of patients with new renal damage in 2 years FU
Antibiotic Prophylaxis

- Side effects

- Overall 38% 5yr incidence of breakthrough UTIs despite prophylaxis in those with severe VUR

- ? Fu VCUG
Medical Management of Vesicoureteral Reflux

When can antibiotic prophylaxis be stopped?

Study* (retrospective)
78 patients treated for m=26 months
Then antibiotic prophylaxis stopped.
Followed for 3 years.

1 patient
8 UTI (cystitis)
No scars

Low risk to discontinue prophylaxis if patient with reflux doing well.

* A. Al-Sayyad et al, J Urol 2005
Bladder Training

- Dysfunctional voiding seen in 20-30% of those with primary VUR

- Dysfunctional voiding associated with
  - greater risk of UTI (> 4 times)
  - Non resolution
  - Renal scar formation

Bladder Dysfunction* and Reflux
Spontaneous Resolution

Without treatment** 11%-33%
(abnormal urodynamics)

With treatment 44%-92%

* Excluding obvious neurogenic bladder patients (i.e., myelodysplasia, sacral agenesis and cloaca patients)
** Anticholinergic, bowel training, bladder training
Indications for Surgical Intervention

- **Absolute**
  - Breakthrough infections on prophylaxis

- **Relative**
  - High grade reflux with scarring at presentation
  - Progressive renal scarring/ decreased renal growth
  - Persistent reflux after puberty
  - Reflux associated with congenital anomalies at the UVJ (e.g., bladder diverticula)
  - Intolerance of surveillance / Poor compliance
Vesicoureteral Reflux

- The Problem of VUR
- Prevention of Surgery
- Surgery or endoscopy
- Optimization of VUR surgery
Surgical Options

- Endoscopic
  - Deflux
  - 83% successful

- Open / Lap techniques
  - 98% successful
  - Intravesical
    - Cohen cross-trigonal
    - Politano-Leadbetter
    - Glenn-Anderson
  - Extravesical
    - Lich-Gregoir
Complications of Endoscopic treatment

- **Persistent VUR**

[Graph showing success rate over cases]

Images A and B showing endoscopic views.

Complications of Endoscopic treatment

- Obstruction
  - Rare: 292 refluxing units treated with Deflux with no hydronephrosis at 12 mos
  - Reports of small numbers with short term, self-limited symptomatic obstruction

- Recurrent VUR (up to 20%)
  - More studies are needed

Complications of Endoscopic treatment

- **Contralateral VUR**
  - Analyzed in recent series of 126 children treated with Deflux for unilateral VUR, grades 1-4, and found new contralateral VUR in 17/126 (13.5%)*
  
  - Higher rates in **girls** under 5 yrs of age
  
  - 2/17 resolved within 6 months, 2 opted for contralateral injection with resolution

Subureteric Injection

**Advantages**
- Minimally invasive
- Day surgery
- Can be repeated
- Rare complications

**Disadvantages**
- Less efficacious than open reimplantation
- Long term safety and efficacy studies for some substances are lacking

Patient Preference?

Cost?
Mean Annual Institutional Reflux Procedures

<table>
<thead>
<tr>
<th>Year</th>
<th>Reimplants</th>
<th>Injections</th>
<th>Total Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>58</td>
<td>17</td>
<td>75</td>
</tr>
<tr>
<td>2003</td>
<td>55</td>
<td>43</td>
<td>98</td>
</tr>
<tr>
<td>2004</td>
<td>50</td>
<td>66</td>
<td>116</td>
</tr>
</tbody>
</table>

Reimplant and Injection Frequencies

# Procedures vs. Age (Yrs)

- **All Reimplant Frequency** (purple)
- **All Injection Frequency** (yellow)

Age ranges from 1 to 13 years.
Consensus of Clinical Guidelines Panel

<table>
<thead>
<tr>
<th>Grade</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>V Unilat or Bilat</td>
<td>6-10</td>
</tr>
<tr>
<td>III-IV Bilat</td>
<td>6-10</td>
</tr>
<tr>
<td>III-IV Unilat</td>
<td>6-10</td>
</tr>
<tr>
<td>I-II Unilat or Bilat</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

Medical

Time (Years)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>V Unilat or Bilat</td>
<td>1-5</td>
</tr>
<tr>
<td>III-IV Bilat</td>
<td>1-5</td>
</tr>
<tr>
<td>III-IV Unilat</td>
<td>1-5</td>
</tr>
<tr>
<td>I-II Unilat or Bilat</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>
Vesicoureteral Reflux

- **The Problem of VUR**
- Prevention of Surgery
- Surgery or endoscopy
- Optimization of VUR surgery
Circumcision for the prevention of urinary tract infection in boys: a systematic review of randomised trials and observational studies.

Singh-Grewal D¹, Maccos JJ, Craig J.

Abstract

OBJECTIVE: To undertake a meta-analysis of published data on the effect of circumcision on the risk of urinary tract infection (UTI) in boys.

DATA SOURCES: Randomised controlled trials and observational studies comparing the frequency of UTI in circumcised and uncircumcised boys were identified from the Cochrane controlled trials register, MEDLINE, EMBASE, reference lists of retrieved articles, and contact with known investigators.

METHODS: Two of the authors independently assessed study quality using the guidelines provided by the MOOSE statement for quality of observational studies. A random effects model was used to estimate a summary odds ratio (OR) with 95% confidence intervals (CI).

RESULTS: Data on 402,908 children were identified from 12 studies (one randomised controlled trial, four cohort studies, and seven case-control studies). Circumcision was associated with a significantly reduced risk of UTI (OR=0.13; 95% CI, 0.08 to 0.20; p<0.001) with the same odds ratio (0.13) for all three types of study design.

CONCLUSION: Circumcision reduces the risk of UTI. Given a risk in normal boys of about 1%, the number-needed-to-treat to prevent one UTI is 111. In boys with recurrent UTI or high grade vesicoureteric reflux, the risk of UTI recurrence is 10% and 30% and the numbers-needed-to-treat are 11 and 4, respectively. Haemorrhage and infection are the commonest complications of circumcision, occurring at rate of about 2%. Assuming equal utility of benefits and harms, net clinical benefit is likely only in boys at high risk of UTI.
First 6-12 months after birth

- No Anti-reflux procedures
- If RI with rec fUTI--- ? urinary diversion
Anti-reflux surgery

- **Open / Lap / Robotic techniques**
  - **Intravesical**
    - Cohen cross-trigonal
    - Politano-Leadbetter
    - Glenn-Anderson
  - **Extravesical**
    - Lich-Gregoir
Anti-reflux surgery
Keys of Successful surgery

- Undiagnosed bladder disease is a common cause of failed ureteral reimplants.

- Excisional tapering of a refluxing megaureter requires careful attention to ureteral blood supply during resection of the redundant ureter and closure of the tapered ureter.
Cohen Cross-trigonal reimplant
Politano-Leadbetter Reimplant
Open Ureteral Reimplantation

- High success rates (95-99%)
- Hospital stay of 2-5 days,
- Extravesical reimplants can be performed as day surgery
- Complications (overall 2%) include
  - Urinary retention (8-15%),
  - Persistent reflux (1-3%),
  - Obstruction (2-4%)
  - Contralateral reflux (5-20%)
Ureteral obstruction
Ureteral obstruction
Ureteral obstruction after Deflux
Persistent VUR 

- Inadequate tunnel
- Diverticulum
- Fistula
Evolution in VUR management

Changes

- Minimally invasive surgery
- Observation off RX
- Aggressive management DES
- Prenatal detection

Improvements

- Decreased surgical morbidity
- Pain management
- Early hospital discharge
- Reduced post-op X-Ray evaluations.
Summary

Key issues
- Infection (febrile)
- Renal scarring

Physiology
- Embryology
- Bladder function
Two New Schools of Thought are Emerging

- **Injection therapy**
  - early (assume 83% success)

- ‘**Forget about it**,’
  - “Wait for 2” Approach?
  - don’t get the studies, treat the infections
Avoid Overtreatment?
Complications Management

Retention
  - Transient?

Obstruction
  - Transient?
  - Persistent obstruction
    - Percutaneous nephrostomy
    - Cystoscopy stent if possible
    - Re-image
    - Reoperative reimplantation

Reflex
  - Continue ABX Wait 6-12 months
  - Persistent low-grade VUR
    - Cystoscopy
    - Deflux
    - Live with VUR off Abx?
  - Re-image
  - Reoperative reimplantation