Longitudinal study of infants with high-grade vesicoureteral reflux

Sofia Sjöström

Department of Pediatrics
Institute of Clinical Sciences
at Sahlgrenska Academy

UNIVERSITY OF GOTHENBURG
List of Publications

I. Sjostrom S., Sillén U., Bachelard M., Hansson S. and Stokland E.,
Spontaneous resolution of high grade infantile vesicoureteral reflux.

II. Sjostrom S., Jodal U., Sixt R., Bachelard M. and Sillén U.,
Longitudinal Development of Renal Damage and Renal Function in Infants With High Grade Vesicoureteral Reflux.

III. Sjostrom S., Bachelard M., Sixt R. and Sillén U.,
Change of urodynamic patterns in infants with dilating vesicoureteral reflux; three year followup.

IV. Sjostrom S., Jodal U., Stokland E., Sixt R., Wahll L., and Sillén U.,
Predictive factors for resolution of high-grade infantile vesicoureteral reflux.-Results of uni and multivariate analyses.
Research questions

• What is the spontaneous resolution rate in dilated infantile VUR and which factors affect the outcome? Can we select patients with a high chance of resolution from those with a low probability of resolution?

• What is the frequency of renal abnormality in dilated infantile VUR and how many have impaired renal function? Can we identify risk factors for deterioration of renal status?

• What are the bladder function characteristics in infantile dilated VUR and do they change during the first years of life? How many develop bladder dysfunction?
Study design

- Prospective longitudinal observational study.
- Eligable; Children with primary dilated vesicoureteral reflux (grade III-V) diagnosed during the first year of life.
- Monitoring of renal status, bladder function and natural course of reflux over time.
## Material

<table>
<thead>
<tr>
<th>Paper</th>
<th>I, II, IV</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>115</td>
<td>114 (94 / 20)</td>
</tr>
<tr>
<td>Sex, N (%) : boys girls</td>
<td>80 (70%)</td>
<td>89 (78%)</td>
</tr>
<tr>
<td></td>
<td>35 (30%)</td>
<td>25 (22%)</td>
</tr>
<tr>
<td>Presentation: prenatal UTI</td>
<td>30 (26%)</td>
<td>30 (26%)</td>
</tr>
<tr>
<td></td>
<td>82 (71%)</td>
<td>84 (74%)</td>
</tr>
<tr>
<td></td>
<td>3 (3%)</td>
<td></td>
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</tbody>
</table>
Grade of VUR at inclusion

Number of patients

Grade III  Grade IV  Grade V

Girls  Boys

Grade III  Grade IV  Grade V
# Methods

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Number of investigations per child Median (range)</th>
<th>Age at first investigation Median months (range)</th>
<th>Follow-up time Median months (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VCM, (VCU) &amp; Free voiding studies</td>
<td>3 (2-5)</td>
<td>2.7 (0.03-12)</td>
<td>36 (2-69)</td>
</tr>
<tr>
<td>Scintigrams (DMSA&amp;MAG3)</td>
<td>4 (1-10)</td>
<td>4.7 (0.2-54)</td>
<td>62 (4-135)</td>
</tr>
<tr>
<td>Clearance (51Cr-EDTA-clearance)</td>
<td>3 (1-11)</td>
<td>7.7 (0.5-72)</td>
<td>53 (1-145)</td>
</tr>
</tbody>
</table>
Results

Complete resolution of VUR in 30 (26%)
Downgrading of VUR to grade I-II in 14 (12%)

**Probability of dilated VUR**

A. Split by grade of VUR at inclusion

B. With or without breakthrough infections

C. With or without bladder dysfunction

Log-Rank test:

- Complete resolution of VUR: $p=0.003$
- Downgrading of VUR: $p=0.003$
- Probability of dilated VUR:
  - All patients: $p=0.003$
  - With or without breakthrough infections: $p=0.003$
  - With or without bladder dysfunction: $p=0.003$
Results

Independent variables negatively associated to VUR resolution in multivariate analyses

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal abnormality</td>
<td>0.43 (0.29-0.63)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Bladder dysfunction</td>
<td>0.36 (0.24-0.53)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Breakthrough UTI</td>
<td>0.49 (0.25-0.97)</td>
<td>0.0397</td>
</tr>
</tbody>
</table>
Conclusion

The spontaneous resolution rate in infantile high-grade VUR:
- Is high (Resolution or downgrading in 38%)
- Is higher in boys during the infant year
- Is negatively associated with breakthrough infections, bladder dysfunction, higher grades of VUR and renal abnormalities.
Conclusion

Multivariate analyses

*Renal damage, Bladder dysfunction* and *Breakthrough UTI*

have shown to be three strong independent factors for prediction of resolution of VUR in multivariate analyses.
Results

Probability of unchanged or deteriorated renal status

Breakthrough UTI, bilateral renal damage and subnormal GFR were predictors for deterioration in renal status. Deterioration was more frequent in prenatally diagnosed patients (p=0.047)
Conclusion

The frequency of renal abnormality in infantile dilated VUR is high (85%). Subnormal renal function is seen in 30%.

Renal status
- Remains unchanged in the majority (82%) during the first years of life.
- Breakthrough UTI, bilateral renal damage and subnormal renal function are predictors for deterioration in renal status.
Results

TYPE OF BLADDER DYSFUNCTION

Bladder dysfunction was found in 48 (42%) of study patients

• HIGH CAPACITY & INCOMPLETE EMPTYING
  34 of 48 (71%)

• OVERACTIVE CONTRACTIONS
  14 of 48 (29%)
In infants with ditated VUR:
- Bladder dysfunction is common.
- The urodynamic pattern changes during the first years of life.
- High pressure and low capacity turns into high capacity with incomplete emptying.
- Bladder dysfunction can only be diagnosed from the second year of life and is seen in almost half of the patients.
General Conclusion

This observational study has resulted in:
- a detailed description of the characteristics and course of dilated VUR in infants.
- a description of changes in urodynamics during the first years of life.
- a description of renal status at inclusion and over time.
- risk factors affecting the outcome have been identified.
Clinical Implications

Our study has provided tools for distinguishing infants with a high chance of spontaneous resolution from those with a high risk of remaining dilated reflux.

The study results can be used to formulate hypotheses for future management of infants with dilated VUR.
Thank You!

The doctoral thesis
Longitudinal study of infants
with high-grade
vesicoureteral reflux
is available on internet

http://hdl.handle.net/2077/20459