A Lack of Efficacy of The Xiao Procedure for Bladder Control in Children With Myelomenigocele and Lipomyelomeningocele: Results of a Prospective, Randomized, Double Blind Study

Gerald Tuite, M.D.
Saint Petersburg, Florida
USA
Disclosures

- Johns Hopkins All Children’s Hospital Foundation Grant
- AANS/CNS Sections on Pediatric Neurosurgery & Spine andPeripheral Nerves

Lack of efficacy of an intradural somatic-to-autonomic nerve anastomosis (Xiao procedure) for bladder control in children with myelomeningocele and lipomyelomeningocele: results of a prospective, randomized, double-blind study

Gerald F. Tuite, MD, Ethan G. Polsky, MD, Yves Homsy, MD, Margaret A. Reilly, PT, Carolyn M. Carey, MD, MBA, S. Parrish Winesett, MD, Luis F. Rodriguez, MD, Bruce B. Storrs, MD, Sarah J. Gaskill, MD, Lisa L. Tetreault, RN, CCRP, Denise G. Martinez, MPH, and Ernest K. Amankwah, PhD

Urological Outcome of the Xiao Procedure in Children with Myelomeningocele and Lipomyelomeningocele Undergoing Spinal Cord Detethering: Results of a Randomized, Prospective, Double-Blind Study

Gerald F. Tuite, Yves Homsy, Ethan G. Polsky, Margaret A. Reilly, Carolyn M. Carey, S. Parrish Winesett, Luis F. Rodriguez, Bruce B. Storrs, Sarah J. Gaskill, Lisa L. Tetreault, Denise G. Martinez and Ernest K. Amankwah
Patients with Spina Bifida
Xiao *et al* (2005): 17/20 (85%) “control of urination and continence”

- Urologist: “The Xiao Procedure”
- “Skin-CNS-Bladder” Reinnervation
- “Scratch and Pee”
- Intra-dural anastomosis (e.g., L5 to S3)
Randomize Patients Undergoing Spinal Cord Detethering

Effect of reinnervation?
Effect of detethering?
Effect of rhizotomy?

2009
Johns Hopkins All Children’s Study

• Professor Xiao supervised initial cases
• Children with MM and LMM undergoing tethered cord surgery
• 20 patients
  • 10 Detethering Only
  • 10 Xiao + Detethering
• 3 year follow-up
  • Both groups stopped CIC and Bladder Active Medications for all 3 years
• Multiple evaluations (1,800 data points/patient)
  • Questionnaires
  • Urodynamics
  • Tests of “Scratch and Pee”
A primary endpoint: scratch leg and demonstrate bladder contractions on urodynamic studies.
Scratch and Measure **Bladder Contractions (>10 cm H$_2$O): Specific or Generalized Response**

- **Xiao Group (D+X)**: 7/9 (D+X) had contractions at some point
- Similar to Xiao (85%)?
Scratch and Measure Bladder Contractions (>10 cm H₂O)

More common in control patients

Scratch-initiated Urodynamic Bladder Contractions were NOT more common in Xiao Group

“Control” (D Only)

“Xiao” (D + X)
The Xiao procedure, compared to Controls (Double Blinded RCT)

Our results do NOT replicate the dramatic results reported by Xiao et al.

- Urodynamic contractions in response to scratching
- Voiding in response to scratching
- Continence: Not one patient continent

<table>
<thead>
<tr>
<th></th>
<th>Control Group</th>
<th>Double Blinded</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>20%</td>
<td>10%</td>
</tr>
<tr>
<td>1 year</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>2 years</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>3 years</td>
<td>10%</td>
<td>10%</td>
</tr>
</tbody>
</table>
Bladder Capacity
Increased more with
Xiao Procedure
Subjective QOL

- Greater improvement in bladder volume in Xiao patients
- More decline in motor function in control group

![Graph comparing quality of life between control and Xiao groups over 1, 2, and 3 years.](image)
Did NOT replicate results of Xiao

• No Improvement with The Xiao Procedure
  • Not continent
  • Could NOT “scratch and pee”
  • Urodynamic bladder contractions were not more common

• Some factors DID improve
  • Better Quality of Life
  • Increased bladder capacity

Effect of Sacral Rhizotomy?
Similar results in Adult Spinal Cord Injury Trials

- 2014, J Urology
- 10 adults, SCI
- No reflex voiding

- 2015,
- 8 adults, SCI
- No voiding
Xiao Procedure **Not** Recommended At This Time

- Some effects the result of sacral rhizotomy
- Need confirmatory animal studies
- Basic Science
Research Nurse Coordinator: Lisa Tetreault
Neurosurgery: Luis Rodriguez, Carolyn Carey, Bruce Storrs, Sarah Gaskill
Urology: Yves Homsy, Ethan Polsky, Mike Reisman, Mark Kolligan
Physical Therapy: Maggie Reilly, Kathleen Thompson
Neurology: Parrish Winesett
Pathology: Ignacio Gonzalez
Nephrology: Sharon Perlman
Statistics: Denise Martinez, Ernest Amankwah, Sharon Ghazarian

Thank You!
Similar results in Adult Spinal Cord Injury Trials

- 2014, J Urology
- 10 adults, SCI
- No reflex voiding

- 2015,
- 8 adults, SCI
- No voiding
Continence

• All patients in both groups remained incontinent throughout the entire study period, requiring diapers and pull-ups at all times.

None!

NOT MORE COMMON IN Xiao Group
★ Urodynamic contractions
★ Voiding
★ Continence
Year 2: Can’t void, very high bladder pressures, kidneys at risk

- Bladder capacity increased by an average of 68%
- 4/8 had significant improvement
- None required augmentation
Scratch and Void During Urodynamics

- 20% TBC
- No useful voiding in any patient
- Certainly no better in D + X

Control | Xiao
---|---
Baseline | 1 year | 2 years | 3 years
20% | 10% | 10% | 10%

Control | Xiao
---|---
Baseline | 1 year | 2 years | 3 years
10%
<table>
<thead>
<tr>
<th>Variable</th>
<th>Tampa Bay Results</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control (D)</td>
<td>Experimental (D+X)</td>
<td>Xiao et al (n=20)</td>
<td>Peters et al (n=10)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(n=10)</td>
<td>(n=9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up</td>
<td>3 yrs</td>
<td>3 yrs</td>
<td>2 yrs</td>
<td>3 yrs</td>
<td></td>
</tr>
<tr>
<td>Weakness</td>
<td>3/10 (30%)</td>
<td>1/10 (10%)</td>
<td>5/20 (25%)</td>
<td>5/13 (38%)</td>
<td></td>
</tr>
<tr>
<td>Ambulatory Status</td>
<td>1/10 worse</td>
<td>0/10 worse</td>
<td>NA</td>
<td>1/13 worse</td>
<td></td>
</tr>
<tr>
<td>Continent at 3 yrs</td>
<td>0%</td>
<td>0%</td>
<td>85%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Urge to urinate</td>
<td>50% to 70%</td>
<td>20% to 56%</td>
<td>85% (no baseline)</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>On CIC</td>
<td>70% to 63%</td>
<td>40% to 60%</td>
<td>0%</td>
<td>100% to 20%</td>
<td></td>
</tr>
<tr>
<td>Scratch/Void 1 yr</td>
<td>0%</td>
<td>0%</td>
<td>85%</td>
<td>78%</td>
<td></td>
</tr>
<tr>
<td>Scratch/Void 3 yr</td>
<td>0%</td>
<td>0%</td>
<td>NA</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>Scratch/Contraction 1 yr</td>
<td>20%</td>
<td>0%</td>
<td>85%</td>
<td>78%</td>
<td></td>
</tr>
<tr>
<td>Scratch Contraction 3 yr</td>
<td>80%</td>
<td>33%</td>
<td>na</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>TBC increase 3 yrs</td>
<td>17 cc</td>
<td>84 cc</td>
<td>Na</td>
<td>78 cc</td>
<td></td>
</tr>
</tbody>
</table>
AN ARTIFICIAL SOMATIC-AUTONOMIC REFLEX PATHWAY PROCEDURE FOR BLADDER CONTROL IN CHILDREN WITH SPINA BIFIDA

CHUAN-GUO XIAO, MAO-XIN DU, BING LI, ZHAO LIU, MING CHEN, ZHAO-HUI CHEN, PING-CHENG, XIAO-NAN XUE, ELLEN SHAPIRO AND HERBERT LEPOR

From the Departments of Urology (C-GX, BL, ZL, MC, Z-HC, FC) and Neurosurgery (M-XD), Tongji Medical College, Xiehe Hospital, Huazhong University of Science and Technology, Wuhan, China, and Division of Biostatistics, Department of Epidemiology and Population Health at Albert Einstein College of Medicine (X-XX), and Department of Urology, New York University School of Medicine (C-GX, ES, HL), New York, New York

ABSTRACT

Purpose: Neurogenic bladder is a major problem for children with spina bifida. Despite rigorous pharmacological and surgical treatment, incontinence, urinary tract infections and upper tract deterioration remain problems. The aim of our study was to evaluate the ability to establish and maintain a normal bladder control surgically in patients with spinal cord injury with this procedure.

Materials and Methods: Twenty patients were treated with surgical bladder augmentation. All procedures were performed under general anesthesia. A 12F indwelling cystostomy was placed, and a suprapubic catheter was inserted. After the bladder became filled with about 300 ml, the cystostomy was removed, and the patient voided. The procedure was repeated next day. A 10 mm catheter was inserted into the bladder. Five of the 6 patients with detrusor hyperreflexia with outflow obstruction were treated with periurethral injection of onabotulinum toxin A. Urodynamics were performed before and after treatment. The post-void residual urine declined from 208.71 ml to 71.76 ml, and the capacity increased from 94.33 ml to 177.83 ml. The mean post-void residual urine declined from 70.17 ml to 23.67 ml. Overall, 3 patients failed to exhibit any improvement.

Conclusions: The artificial somatic-autonomic reflex arc procedure is an effective and safe treatment to restore bladder continence and reverse bladder dysfunction for patients with spina bifida.

- 20 children with spina bifida
- Increase in bladder capacity
- Resolution of DESD
Outcomes of Lumbar to Sacral Nerve Rerouting for Spina Bifida

Kenneth M. Peters, Benjamin Girdler, Cindy Turzewski, Gary Trock, Kevin Feber, William Nantau, Brian Bush, Jose Gonzalez, Evan Kass, Juan de Benito and Ananias Diokno

From the Ministrell Program for Urology Research and Education (MPURE), and Department of Urology IXMP, BG, CT, KT, JG, ER, JN, ADI, Department of Clinical Neurophysiology (WN, BB) and Department of Neurology (GTS), William Beaumont Hospital, Royal Oak, Michigan

Purpose: Restoring bladder and bowel function in spina bifida by creation of a skin-central nervous system-bladder reflex arc via lumbar to sacral nerve rerouting has a reported success rate of 87% in China. We report 1-year results of the first North American trial on nerve rerouting.

Materials and Methods: Nine subjects were enrolled in the study. Intradural lumbar to sacral nerve rerouting was performed. Subjects underwent urodynamic testing with stimulation of the cutaneous dermatome and careful neurological followup. Adverse events were closely monitored along with changes in bowel and bladder function.

Results: At 1 year 7 patients (78%) had a reproducible increase in bladder pressure with stimulation of the dermatome. Two patients were able to stop catheterization and all safely stopped antimuscarinics. No patient achieved complete urinary continence. The majority of subjects reported improved bowel function. One patient was continent of stool at baseline and 4 were continent at 1 year. Of the patients 89% had variable weakness of lower extremity muscle groups at 1 month. One child had persistent foot drop and the remainder returned to baseline by 12 months.

Conclusions: At 1 year a novel reflex arc with stimulation of the appropriate dermatome was seen in the majority of subjects. Improvements in voiding and bowel function were noted. Lower extremity weakness was mostly self-limited, except in 1 subject with a persistent foot drop. More patients and longer followup are needed to assess the risk/benefit ratio of this novel procedure.

- Xiao performed the operations
- 7/9 (78%) “reproducible increase in bladder pressure with scratching”
- 2/9 were able to stop CIC
- NO patient was continent
Only two or three patients recruited
Detailed report never published
L5 ventral root (motor)

L5 dorsal root (sensory)

Head

S3 root
Artificial skin–CNS–bladder reflex pathway methods

Patients with Spina Bifida
Xiao et al (2005): 17/20 (85%) “control of urination and continence”

Ventral root of somatic nerve (L5) to ventral root of bladder nerve (S3)

Re-route a reflex arc: “Skin-CNS-Bladder”

Nerve Transfer Procedure
Bladder volume increases with age up to age 13:

\[ \text{EBC} = (30 \times [\text{age in yrs} + 1]) \]

Hjalmas, K, Scand J Urol Nephrol, 1976

Bladder Capacity Increased more with Xiao Procedure

UTI's in the last 3 months
✓ MM and LMM
✓ **Undergoing detethering**
✓ Neurogenic bladder
✓ Can’t control urination
✓ Incontinent

**Exclusion:**
- Unwilling to randomize
- Bladder surgery
- Live outside our area

**Stop CIC**
**Stop Medications**

- Test voiding
- Urodynamics
- Neurologic Evals

**Randomization in OR**

**Detethering**

(D + X) – (D) = X

**Repeat for 3 yrs**

**Patients and Evaluators Blinded**

**Scratch Dermatome**

**Scratch Dummy Dermatome**

D

D + X
Artificial skin–CNS–bladder reflex pathway methods


Patients with Spina Bifida

Xiao et al. (2005): 17/20 (85%) "control of urination and continence"

Randomize Patients Undergoing Spinal Cord Detethering

Nerve Transfer Procedure
Re-route a reflex arc: "Skin–CNS–Bladder"

Detethering?
Nerve Sectioning?