Overview of Fetal Urological Surgery
Indications, Outcomes and Ethical Issues

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FETAL LOWER URINARY TRACT OBSTRUCTION (LUTO)

• Occurs due to outflow obstruction of the bladder during fetal urinary tract development (bladder wall thickening, hydronephrosis, and renal damage)

• Injury is too early and many times associated with renal dysplasia
• Fetal LUTO affects approximately 2–3 out of every 10,000 fetuses

• Wide spectrum of morbidity associated with LUTO

Three main diagnoses:

• Posterior urethral valves (PUV)
• Urethral atresia
• Prune belly syndrome

• Other: anterior urethral valves, megalourethra, megacystis-microcolonhypercystis syndrome, cloacal malformations, and prolapsing cecoureterocele

Anumba et al, 2005 / Heihhila et al 2011
• Most common cause of LUTO (approx. 1/8000 live male births)

• Up to 28% of boys with PUV maintain a lifetime risk for ESRD

• PUV: most common cause of bilateral hydronephrosis in males

• Fetal US:
  - Distended bladder, thickened detrusor, posterior urethral dilatation (key hole sign)
  - Oligohydramnios
  - Severe hydroureteronephrosis (renal cysts)
• Severe cases, mortality up to 45%

• Postnatal: severe morbidity and mortality, independent of treatment type
• Incidence: 3.8/100,000 live male births

• Triad: intra-abdominal testes, urinary tract dilatation and, laxity of the anterior abdominal wall

• A true functional urethral obstruction is usually absent (prostatic hypoplasia) leading reduced urine outflow
URETHRAL ATRESIA

• Rare: estimated to occur in 0.3 per 10,000 live births

• Most fetuses with urethral atresia do not survive

• Unless a site of drainage is present such as a patent urachus or fetal intervention

OTHER FETAL RADIOLOGIC EVALUATION

Ultrafast T2 sagittal MRI: left MCDK (arrow) in a 21-week-old fetus

3D-US, fetal bladder at initial evaluation (vol. 180 mL)

Fetal bladder 48 h after vesicocentesis (vol. 30 mL)


Cochrane Miller J., Radiology rounds, 11, 6, June 2013
Prenatal Intervention: Options

- Pregnancy termination
- Open fetal surgery
- Fetal serial vesicocentesis
- Percutaneous vesicoamniotic shunt (VAS) placement
- Fetal cystoscopic procedures
Pediatric urologists do provide:

- Prenatal council as part of a multidisciplinary team who is making such decisions
- Care for postnatal issues that can arise following intervention

Most urologists in the USA do not actively participate in Prenatal Intervention
• Prenatal diagnosis: source of distress to parents and health professionals too

• The question: increased surveillance, diagnosis and intervention is beneficial, and if so, to whom?

Anna Smajdor, J Med Ethics 2011;37:88
• In fetal surgery, mother and fetus become patients

• Is it ethically acceptable to impose the risks of surgery on someone who stands to derive no clinical benefit?

PRENATAL INTERVENTION: ETHICS

• Key: identify those fetus that would not survive with postnatal therapy alone

• Role informed consent and respect for autonomy very complicated

Informed Consent: Success of Intervention

• Parents need to understand that at the outset of fetal intervention:

  • some fetuses will not survive despite intervention
  
  • those that do may be at increased risk for renal morbidity
Overwhelmingly, VAS placement is the most common procedure with the largest dataset to analyze.
• Most severe fetal complication and cause of perinatal mortality

• VAS: ameliorate pulmonary hypoplasia

• AF levels are critical for proper lung development during the canalicular phase (between weeks 16 and 24)

Smith LJ. Paediatr Respir Rev. 2010;11(3):135–42
PRENATAL VAS (PLUTO)

• Randomised women (UK, Ireland, and Netherlands) whose pregnancies were complicated by LUTO

• Randomly assigned to receive either the intervention (VAS) or conservative management

31 women (16 VAS – 15 CM)

- Survived to 28 days:
  - **VAS**: 8/16 (50%)
  - Conservative management: 4/15 (26.5%) (intention-to-treat relative risk [RR] 1.88, 95% CI 0.71–4.96; p=0.27)

- All 12 deaths were caused by pulmonary hypoplasia

Overall outlook in both trial groups at 2 years was poor (only 2 babies surviving without renal impairment)

• VAS improves perinatal survival (long-term renal function is unclear)

(Morris et al, Lancet 2013; 382: 1496–506)
Prenatal Intervention: Results

- Updated meta-analysis (2017): 112 fetuses with VAS - 134 treated conservatively

- VAS improved perinatal survival (from birth up to 6 months of age) (57% VAS v. 39% conservative treatment)

- 2-year renal function outcomes, VAS placement did not improve postnatal renal function

Outcome data for fetal cystoscopy are limited (fewer centers performing this procedure)

2016 single institution retrospective study (30 male fetuses)

Authors theorize that cystoscopy improved specificity of diagnosis and improved selection of fetuses with PUV for VAS placement

• **VAS** literature, complication rate is approximately 40%
  • Shunt dislodgement, migration or blockage, fetal ascites, premature rupture of membranes, preterm labor, shunt site abdominal wall herniation, and, in some instances, fetal demise

• **Fetal cystoscopy**, complications in one series included recurrence of obstruction (20%), uro-rectal or vesicocutaneous fistula (13%), need for repeat procedure, premature rupture of membranes, and fetal demise

Prenatal renal parenchymal area as a predictor of early end-stage renal disease in children with vesicoamniotic shunting for lower urinary tract obstruction.


- Retrospective study of 15 male fetuses (01/2009 and 12/2015) with LUTO who survived VAS placement

- Diagnoses included: PUV (8), PBS (4), urethral atresia (2), and megacystis microcolon intestinal hypoperistalsis syndrome (1)
• There are limited prognostic tools available during gestation to evaluate and predict postnatal renal function

Fetal urine should become more hypotonic as gestation progresses and electrolytes are reabsorbed by the fetal kidney (urinary Na < 100mEq/L, Cl < 90mEq/L, osm. < 200mEq/L, β₂-microglob. < 6 mg/L) (Nicolini and Spelzini, 2001)

Serial sampling are used to triage prenatal intervention and predict postnatal renal risks.

Not very clear diagnostic accuracy of these tests. Morris RK, et al. Prenat Diagn. 2007;27:900
• Analyze renal parenchymal area (RPA) in fetuses with LUTO and, its use as a predictor of postnatal renal function

• Shunts were placed at 21.39 ± 3.58 weeks of gestation

Patients were divided into 2 groups according to renal function in the last follow-up:

- **Group 1, ESRD**: 8 patients (53.3%)
- **Group 2, non-ESRD**: 7 patients (46.7%)

Prenatal US of a 22wk fetus with LUTO before VAS placement

A) Total renal area measurement (cm$^2$)  B) Area of hydronephrosis (cm$^2$)

Mean Renal parenchyma area was significantly smaller in patients with ESRD (p<0.05)

• Even with early VAS, postnatal morbidity remain high, emphasizing role of renal dysplasia, in postnatal renal failure

• Prenatal RPA measurement could have an important role as a non-invasive tool to predict postnatal renal function

Prenatal VAS: Conclusions

• From SRs and data from PLUTO trial, VAS increase early survival rates in patients with an initial poor prognosis.

• Interventions do not have significant benefit on renal function.

• “Renal Dysplasia”, insult is to early and led to postnatal renal failure.
POSTNATAL MANAGEMENT
PUV – ENDOSCOPIC VALVE ABLATION

• Cystoscopy: 6.5 - 7.5 - 9-Fr.

• Laser Fiber

• Bugbee Electrode

• Resectoscope 9.5-Fr with Collins knife
PUV – ENDOSCOPIC VALVE RESECTION
Goal

• Evaluate efficacy of PUV resection during early postnatal period

• Compare results between premature/low weight babies and term neonates
2004 - 2015, 130 patients underwent endoscopic PUV resection

44 neonates (< 28 days), divided in 2 groups:

- Group 1 (n=25): premature (<37 wks) / low weight (<2.5 Kg)
- Grupo 2 (n=19): term / weight >2.5 Kg
# PUV Endoscopic Resection: Neonates

## Results

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<th>Group 1</th>
<th>Group 2</th>
<th>p-value</th>
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<tr>
<td>Median age surgery (days)</td>
<td>7</td>
<td>7</td>
<td>0.910</td>
</tr>
<tr>
<td>Time to follow up (months)</td>
<td>71.4 ± 39.1</td>
<td>57.6 ± 34.2</td>
<td>0.230</td>
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<td>Initial mean serum Cr (mg/dL)</td>
<td>2.19 ± 1.53</td>
<td>1.1 ± 0.62</td>
<td>0.004</td>
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<td>Initial mean eGFR (mL/min per 1.73m²)</td>
<td>11.4 ± 7.4</td>
<td>23.7 ± 15.1</td>
<td>0.003</td>
</tr>
<tr>
<td>Follow-up nadir Cr (mg/dL)</td>
<td>1.18 ± 1.31</td>
<td>0.50 ± 0.45</td>
<td>0.030</td>
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<tr>
<td>eGFR at last follow-up (mL/min per 1.73m²)</td>
<td>78.1 ± 52.3</td>
<td>118.2 ± 54.3</td>
<td>0.020</td>
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Podium Presentation, Fall Meeting SPU, Montreal, September 2017
• Elevated serum creatinine in Group 1

• No other significant differences between the 2 groups (RVU, hydronephrosis, redo valves resection, urethral stenosis)
Conclusion

• PUV resection is a safe an effective surgical option in premature and low weight babies

• Preterm/Low birth weights boys had a worse initial and 1 year renal function when compare with term neonates
In 2011, randomized controlled trial outcomes of prenatal versus postnatal repair of MMC

183 women were randomized: 91 to prenatal open surgery and 92 to postnatal surgery

• Prenatal repair reduced need for VPS at 12 months (40 vs. 82%)

• Improved score for mental development and motor function at 30 months of age

It also has disadvantages: premature birth, fetal or neonatal death, and uterine complications.

Prenatal myelomeningocele repair: Do bladders better?


• 16 pts (8 pre / 8 postnatal MMC repair) with postnatal follow-up of > than 2 years

• Neurogenic bladder (CIC and anticholinergic) was seen in 50% in the prenatal and in 100% in the postnatal group
Effect of Prenatal Repair of Myelomeningocele on Urological Outcomes at School Age (SPU Fall Meeting, Atlanta, September 2018)


- 156 children (78 pre- and 78 post-natal) had urologic examinations
- Mean age at follow-up in both groups was 7.4 years
- Required CIC: prenatal surgery group (61.5%) compared with (87.2%) of the children in the postnatal group (Relative Risk (RR) = 0.71)
Prenatal Treatment: Spina Bifida

- **Effect of Prenatal Repair of Myelomeningocele on Urological Outcomes at School Age** (SPU Fall Meeting, Atlanta, September 2018)
  

- **Volitionally voiding**: prenatal repair (24%), postnatal (4.2%) (RR 5.8, 95% CI 1.8 - 18.7)

- No statistical differences in others such as, augmentation cystoplasty, vesicostomy, and, videourodynamic data or findings on renal/bladder ultrasound
FETAL INTERVENTION: CONCLUSIONS

• Ability to intervene during fetal development has been a reality for several decades

• Several challenges remain and specifically include:
  • improving the accuracy of the prenatal evaluation
  • determining the ideal patient for intervention
  • most effective and least morbid intervention technique
Thanks...

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