Welcome to

ERKNet/ESPN
Educational Webinars on Pediatric Nephrology & Rare Kidney Diseases

WEBINAR
18/01/22

Posterior urethral valves

Speaker: Michal Maternik (Gdansk, Poland)

Patient voice: Marco & Francesca Giorgetta (Milan, Italy)

Moderator: Francesco Emma (Rome, Italy)

ERKNet
The European Rare Kidney Disease Reference Network

european society for paediatric nephrology

Patient's Voice – Andrea Giorgetta

- Andrea is a (almost) 3yo boy
- Chronic Kidney Disease (CKD) as a consequence of PUV diagnosed pre-birth
- During a routine scan (week 31), low amniotic fluid (anhydramnios) and suspected renal dysplasia, sent to prenatal diagnosis. 4 weeks prior, amniotic fluid was normal
- Analysis indicated likely PUV due to kidney situation, enlarged ureters and bladder
- The equipe including urologists, nephrologists and gynecologists agree to attempt an amnioinfusion, only to exhibit in a few days renewed anhydramnios
- Next, relevant decision, chose between (i) fetal surgery to apply a shunt and (ii) induce premature birth to allow treatment
- The decision was on us: not easy, but opted to induce birth (week 33+0)

First weeks

- Fortunately, good weight and size (2.5kg)
- Unfortunately, some premature-birth complications keeping Andrea in ICU and pathology care unit for 2 months, including surgery for removing the obstruction
- Vivid memory of a meeting with nephrologists and urologists, where we understand maybe for the first time the prognosis, with likely need of dialysis and transplant
  - *“Possible scenario”: creatinine stabilizing >1.5[mg/dL], i.e. short time ahead*
  - *“Likely scenario”: between 0.5 and 1.5, i.e. 10-20 years ahead*
  - *“Possible, but unlikely, scenario”: lower than 0.5, i.e. potentially normal life*

Our questions at the beginning

- Will the baby live?
- Will he have a normal childhood?
- Will he need dialysis and a transplant? By when?
- Why don’t we make more frequent tests?
- What does it mean that we have to wait and see how things evolve?
- What can we expect in the short term, medium term, and long term?
- How is it possible that there is nothing that we can do?

Where we are today

- Approx. 6-monthly checks
- Andrea is fairly stable at c. 0.7 [mg/dL] of creatinine, decent electrolytes (except potassium), no urinary tract infections so far despite reflux - he is under antibiotic prophylaxis; urologic system to be re-assessed after toilet training
- He is growing (95cm height, 15kg weight at almost 3yo) and we are aware that, given the initial situation and compared with other baby patients, he is doing well…
- …but we are conscious that it is likely a matter of time
- As parents the future outlook is clearly our top concern and we try to do the best we can to make even the smallest good

Our questions today

- What diet regime should we follow? How strictly?
- Can the child have a normal childhood (school, sport, etc.)?
- What can we expect for the future, and when?
- Should CKD worsen, how sudden would it happen?
- What else can we do?
- Should we do anything already as potential future donors?
- Is Covid-19 a specific risk for him?
- Where is R&D going to regarding CKD?

Some learnings, considerations, suggestions

- We are not used to this. It all happened in a few days and we have a hard time understanding what is happening. Every single word sticks in our mind and we build on it. Clarity of communication is key.
- Help in choices is key for us (e.g. fetal surgery vs. induced birth was tough).
- The “wait & see” is very difficult to understand initially. The more we can understand the “process”, even if it is multi-year and subject to a lot, the better we feel.
- In today’s world, patients (parents) can be easily confused by information. Help in managing information is useful, depending on the type of parent: some need psychological support, particularly in delicate moments, some need data, some need reading and information.
- Parents are ready to do and give anything, literally. Feel free to ask.

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PUV – presentation outline

1. Incidence
2. Pathophysiology
3. Antenatal diagnosis and treatment (indications for intervention)
4. Postnatal diagnosis
5. Postnatal management
6. CKD, ESRD in patients in PUV
7. Bladder dysfunction: diagnosis and management
8. Late presentation of PUV
9. Transplantation in children with PUV

LUTO – Lower Urinary Tract Obstruction

Total prevalence of prenatally detected LUTO

3,34 per 10 000 births

Live births prevalence with LUTO

2,24 per 10 000 births

DOI: 10.1111/j.1471-0528.2012.03476.x
www.bjog.org

Congenital lower urinary tract obstruction: a population-based epidemiological study

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Correspondence: Dr M Kilby, Academic Department, Theme of Reproduction, Genes and Development, School of Clinical and Experimental Medicine, College of Medicine and Dentistry, University of Birmingham, Birmingham, B15 2TT, UK. Email m.d.kilby@bham.ac.uk

Accepted 7 July 2012. Published Online 24 August 2012.

Table 1
LUTO subtype with prevalence.

LUTO subtype	Complex	Isolated	Total	%LUTO	Prevalence (95% CI)
Posterior urethral values	19	160	179	63.0%	2.10 1.79–2.41
Urethral atresia	18	10	28	9.9%	0.33 0.21–0.45
Urethral stenosis	4	16	20	7.0%	0.23 0.13–0.34
Prune belly syndrome	5	2	7	2.5%	0.08 0.02–0.14
LUTO other	0	2	2	0.7%	0.02 0.00–0.06
LUTO unspecified	17	31	48	16.9%	0.56 0.40–0.72
Total LUTO cases	63	221	284	100.0%	3.34 2.95–3.72

Incidence

The calculated incidence for PUV is 1/3800 male births per - year

The proportion of PUV presenting according to age was:

- antenatally (n = 40, 35%),
- infancy (n= 47, 42%),
- late (n = 26, 23%)

Diagnosis:

33% under age of 1 month, 33% in the first year, 33% thereafter

(Parkhouse HF 1988),

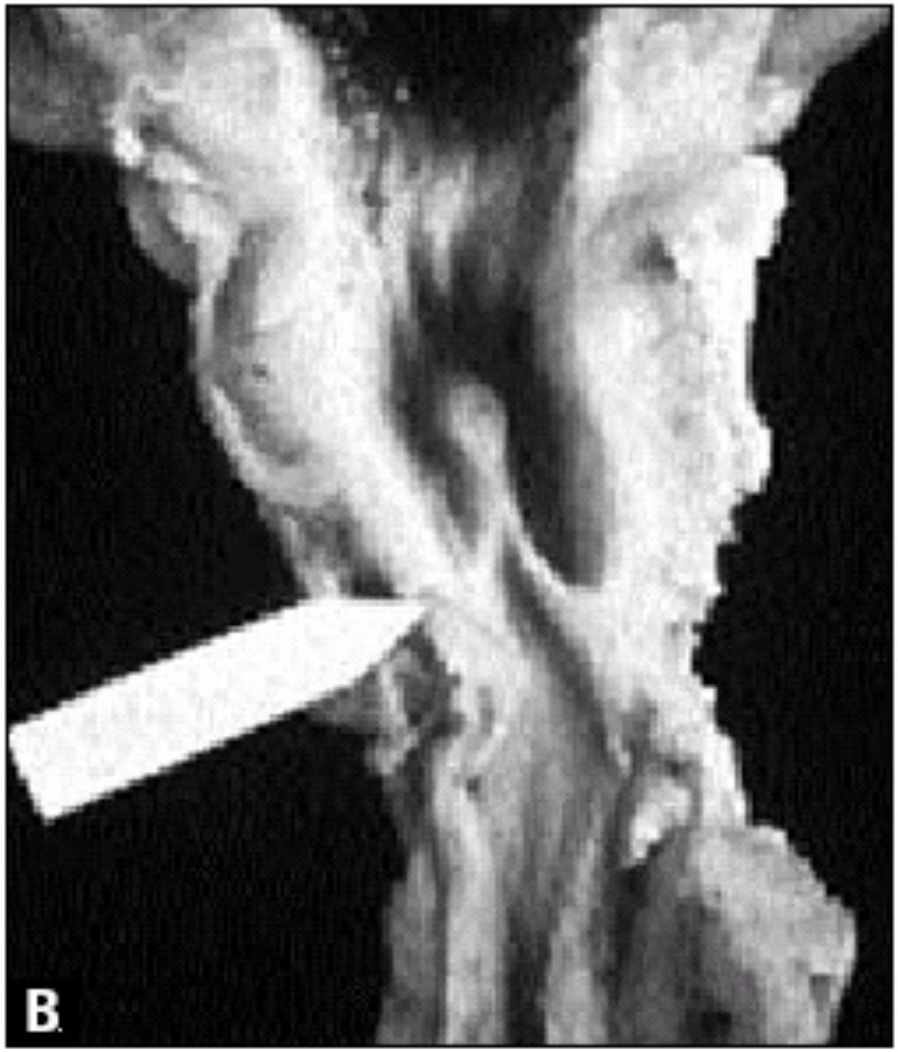
Current epidemiology and antenatal presentation of posterior urethral valves: Outcome of BAPS CASS National Audit

E. Brownlee et al. Journal of Pediatric Surgery 54 (2019) 318–321

Anatomy

Typical – 95% - Posterior urethral folds which arise from the caudal verumontanum along the lateral margins of the urethra fuse anteriorly causing an obstruction.

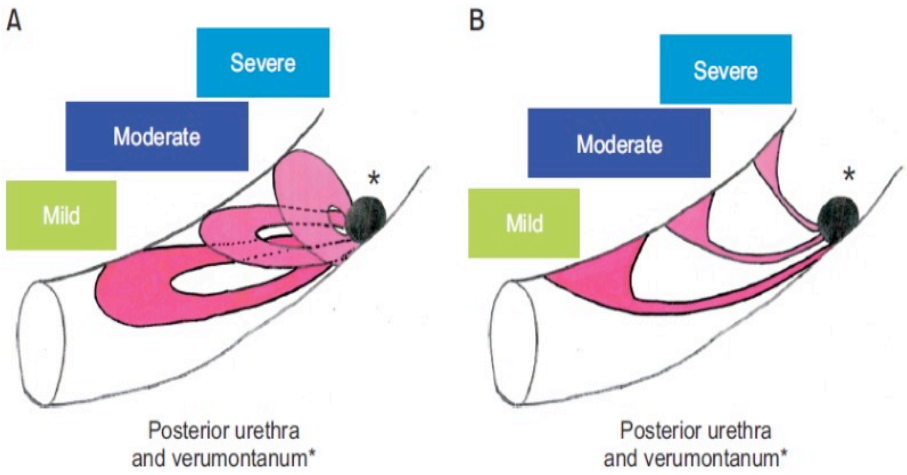
Atypical - 5% -Round membrane at the caudal verumontanum with a hole in the middle that is either above the verumontanum or below it.



Anatomy

(A) Lateral view of posterior urethral valve (PUV) type 1, illustrating that the milder the lesion the bigger the posterior defect (hole) and more distally located anterior fusion.

(B) Lateral view of PUV type 1, illustrating that the milder the lesion the thicker the anterior lesion.



Review Article
Investig Clin Urol 2017;58 Suppl 1:S46-53.
https://doi.org/10.4111/icu.2017.58.S1.S46
pISSN 2466-0493 • eISSN 2466-054X

INVESTIGATIVE AND CLINICAL UROLOGY
ICUROLOGY

Aggressive diagnosis and treatment for posterior urethral valve as an etiology for vesicoureteral reflux or urge incontinence in children

Hideo Nakai, Taiju Hyuga, Shina Kawai, Taro Kubo, Shigeru Nakamura
Department of Pediatric Urology, Aichi Medical University Children's Medical Center Tochigi, Shimotsuke, Japan

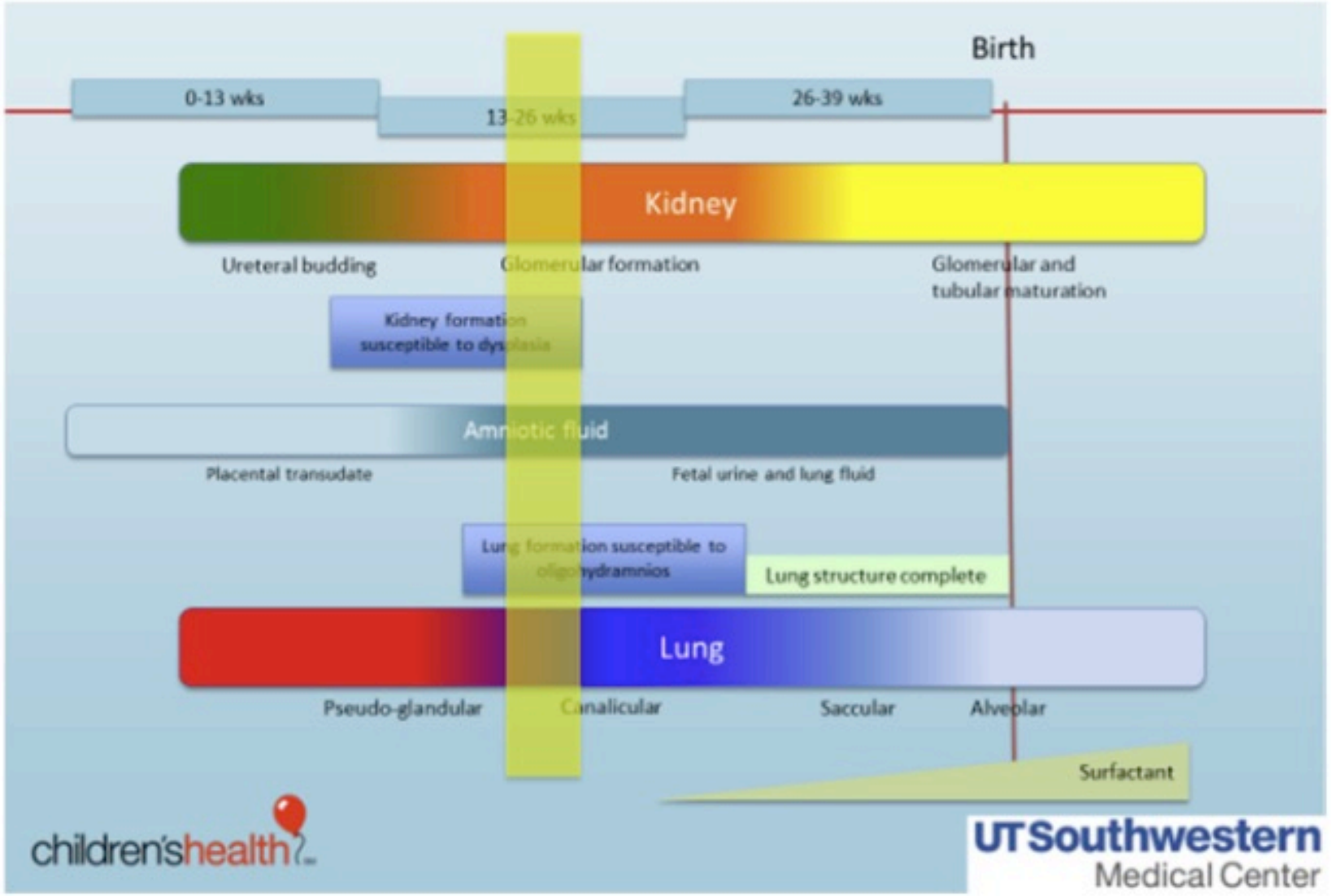
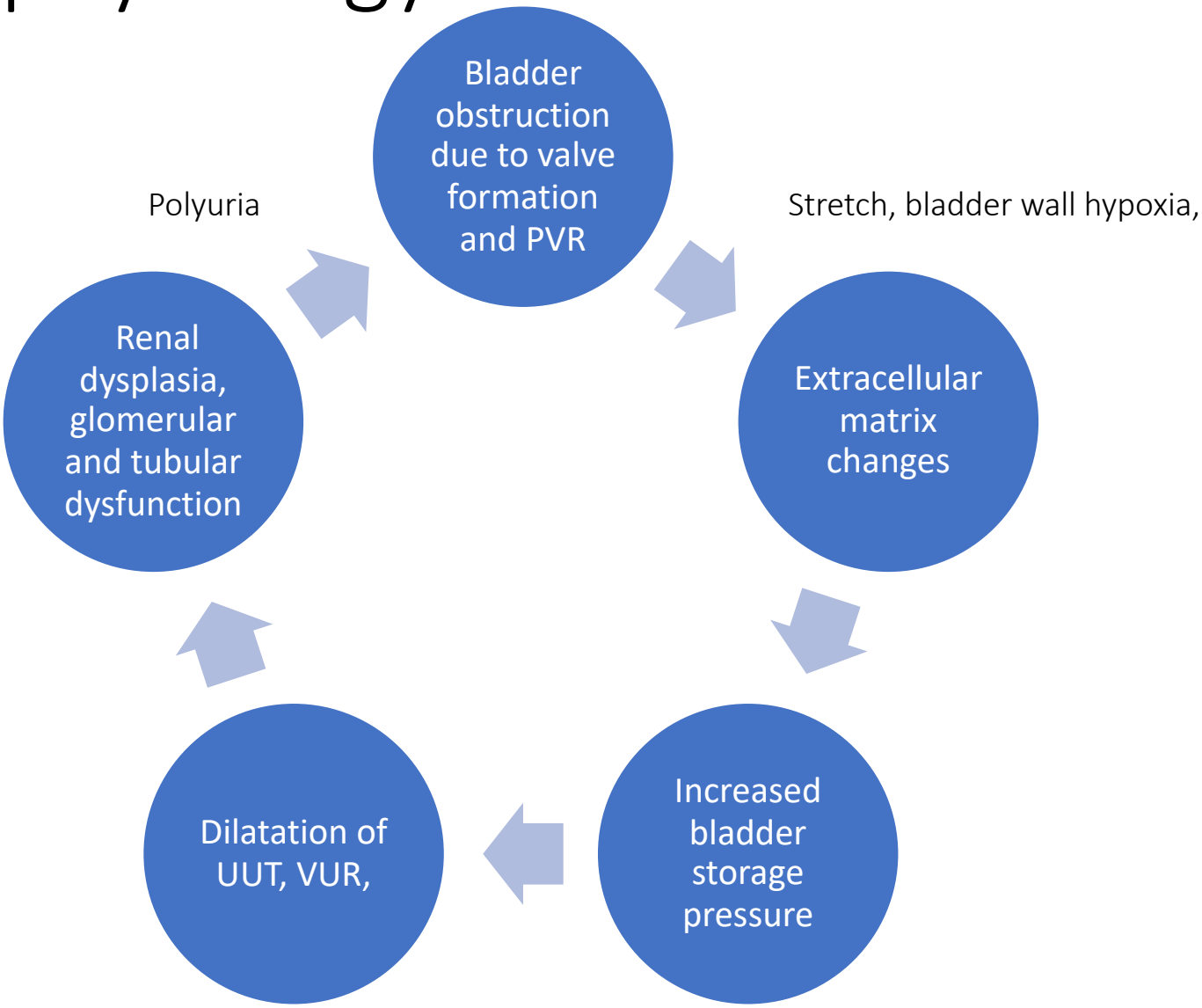


Figure 3 Renal and pulmonary co-development [15].

[15] Peters CA, Reid LM, Docimo S, Luetic T, Carr M, Retik AB, et al. The role of the kidney in lung growth and maturation in the setting of obstructive uropathy and oligohydramnios. J Urol 1991;146:597–600.

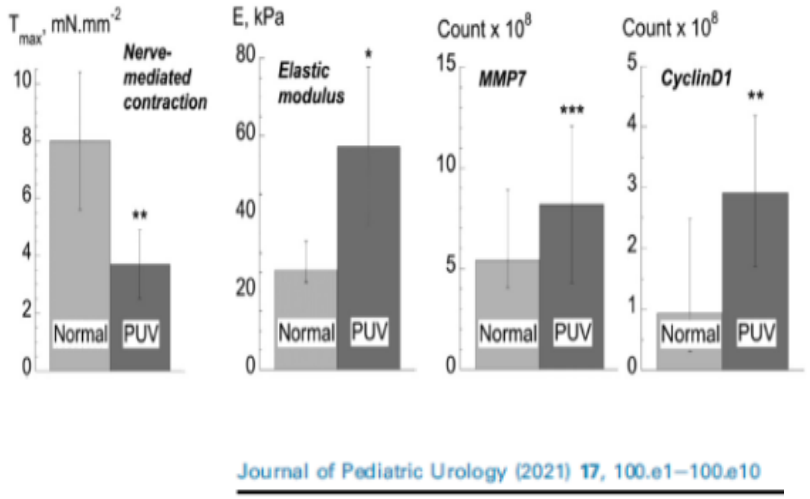
Pathophysiology



PUV Bladder consequences

Obstruction consequences for bladder:

- Hypertrophy of smooth muscles and increase in deposition of extracellular matrix (influence on passive and active properties of bladder wall)
- Reduction in contractile capacity of the smooth muscles
- Need for generation of higher pressures to pass urine



Journal of Pediatric Urology (2021) 17, 100.e1–100.e10

Pathogenesis

- Unilateral VUR (Hoover 1982)
- Urinary extravasation (Keafer 1995)
- Patent urachus, (Adzick 1985),
- Large bladder diverticulum (Cass 1981, Rittenberg 1988)

MAY BE PROTECTIVE BY LEADING TO DECOMPENSATION OF HIGH PRESSURE.

Patomorphology

Primary malformations: mesenchymal or cartilage tissue premature tubuli and glomeruli. – primary renal dysplasia

Secondary malformations: renal cortical atrophy, interstitial fibrosis and interstitial nephritis

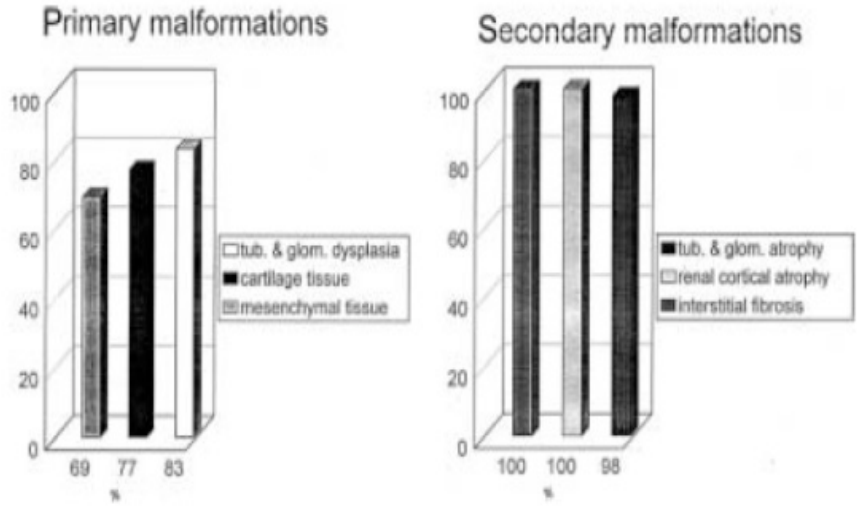


Fig. 3 Histological findings

Frank-Martin Haecker · Manfred Wehrmann
Hans-Walter Hacker · Gerhard Stuhldreier
D. von Schweinitz

Renal dysplasia in children with posterior urethral valves: a primary or secondary malformation?

Pediatr Surg Int (2002) 18: 119–122

Pool question

Are you involved in prenatal counselling of patients with LUTO in your Center:

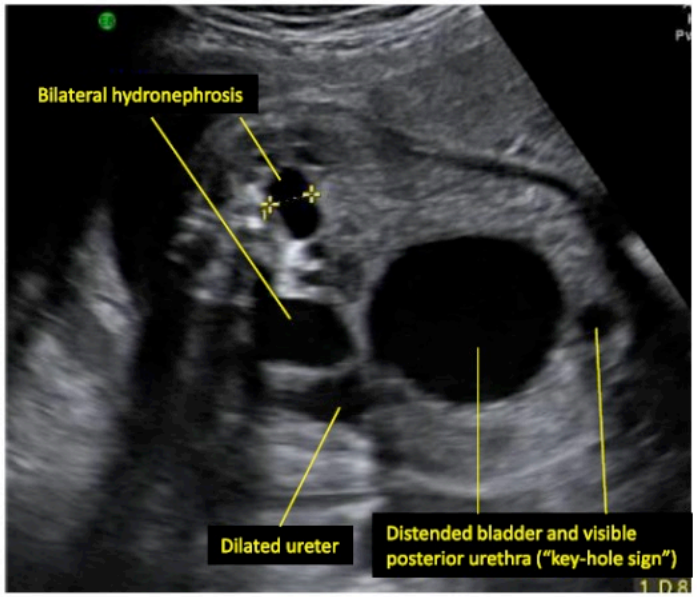
A. Yes
B. No

Antenatal diagnosis – ultrasound

Table 1
Clinical score for antenatal diagnosis of LUTO [7].

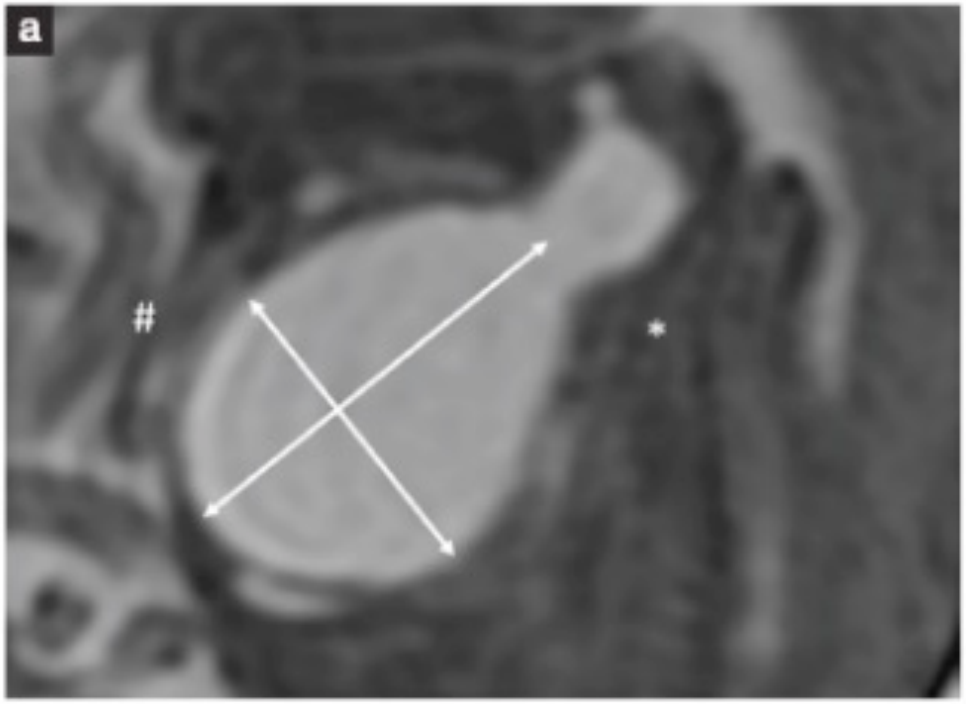
Ultrasound signs	Points
Severe megacystis (volume > 35 cm^3 or ascites)	4
Bilateral ureteral diameters	1.3 for each mm of ureteral size
Oligo- or anhydramnios	4
Fetal sex (male)	4
Referral before the 28th week	4

	Risk of LUTO	Sensitivity
Score ≥ 9.5	96%	78% (70–85)



Fontanella F Ultrasound Obstet Gynecol 2018; 52: 739–743

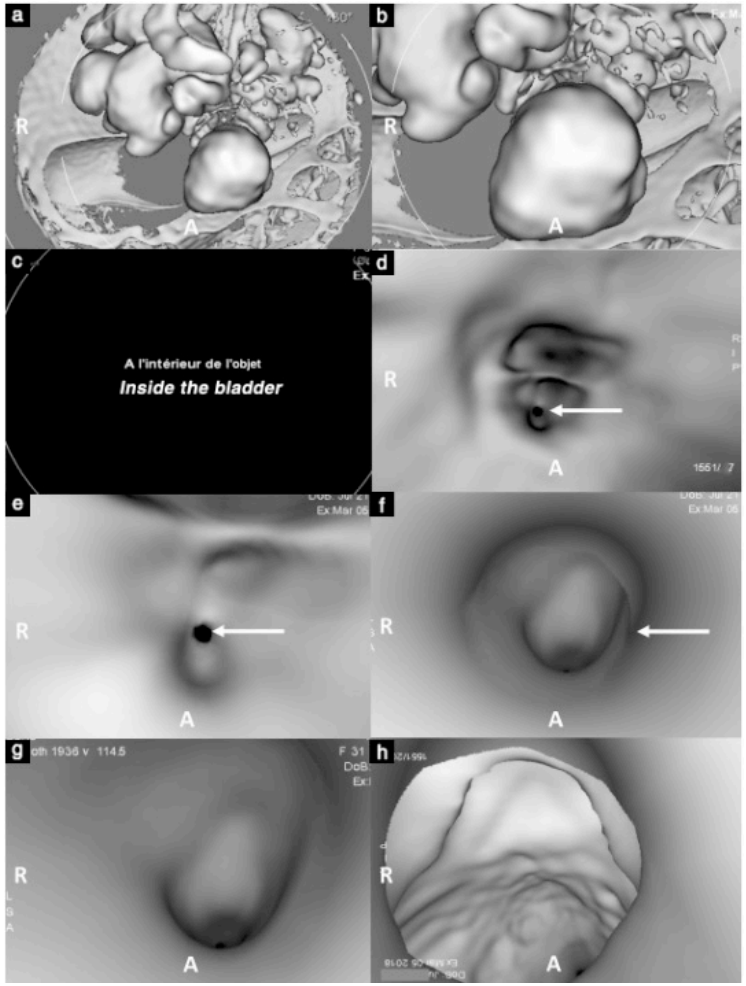
Antenatal diagnosis – MRI



Ultrasound Obstet Gynecol 2020; **56**: 86–95
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.20297

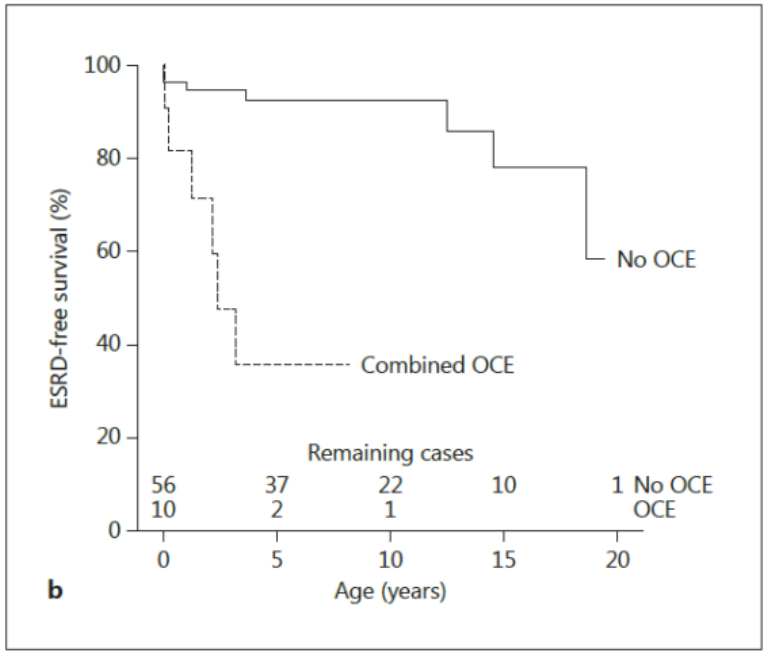
Biometric and morphological features on magnetic resonance imaging of fetal bladder in lower urinary tract obstruction: new perspectives for fetal cystoscopy

N. VINIT[1,2], D. GREVENT[2,3,4], A.-E. MILLISCHER-BELLAICHE[2,3], V. M. PANDYA[5], P. SONIGO[2,3], A. DELMONTE[6], S. SARNACKI[1,6,7], Y. AIGRAIN[1,7], N. BODDAERT[3,4,7], B. BESSIÈRES[8], G. BENCHIMOL[5], L. J. SALOMON[2,5,7], J. J. STIRNEMANN[2,5,7], T. BLANC[1,2,7] and Y. VILLE[2,5,7]



Prenatal anatomical predictors of ESRD

- Megacystis –bladder volume cutoff of 5.4 cm3, (Fontanella - 2018)
- Oligohydramnios
- Increased parenchymal echogenicity
- Cystic changes in the kidney parenchyma
- RPA - renal parenchymal area (Moscardi R – J Ped Urol 2018)



Matsell D Fetal Diagn Ther 2016;39:214–221

Prenatal biochemical predictors of ESRD

- β2-microblobulin and chloride (93% sensitivity and 71% specificity) in differentiating CKD1+2 vs CKD 3-5 – after 10 years of age
- Measuring the Amniotic Fluid abundance of 67 peptides of Foetal Urine origin allowed prediction of postnatal renal survival in foetuses with posterior urethral valves. Sci Rep2020 Dec 10;10 (1):21706

Table 1 Fetal urine biochemistry

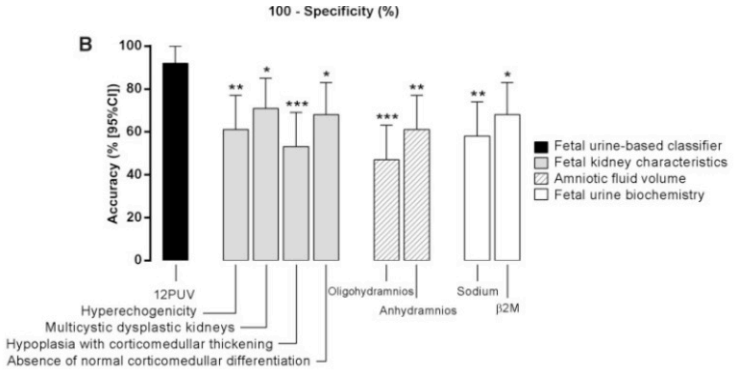
Parameter	Favorable value
Sodium	<100 mmol/L
Calcium	<8 mg/dL
Chloride	<90 mmol/L
Osmolality	<200 mmol/L
Total protein	<20 mg/dL
β-2 microglobulin	<6 mg/dL

How to cite this article: Dreux S, Rosenblatt J, Moussy-Durandy A, et al. Urine biochemistry to predict long-term outcomes in fetuses with posterior urethral valves. *Prenatal Diagnosis*. 2018;38:964–970. https://doi.org/10.1002/pd.5359

Prenatal biochemical predictors of ESRD

The 12 peptide signature from **foetal urine** predicted postnatal renal outcome (early ESRD) for suspected PUV cases with a sensitivity of 88%, a specificity of 95%

Ongoing ANTENATAL multicentre European trial - validation of a foetal urine peptidome-based to predict postnatal renal function in PUV.



Klein J, Lacroix C, Caubet C (2013) et al. Sci Transl Med

Antenatal intervention

Table 2 Staging of lower urinary tract obstruction (LUTO) based on bladder volume at referral and gestational age at appearance of oligo- or anhydramnios

LUTO stage	*Definition*
Severe	Bladder volume $\geq 5.4\,cm^3$ and/or oligo- or anhydramnios before 20 weeks
Moderate	Bladder volume $< 5.4\,cm^3$ and/or normal AFV at 20 weeks
Mild	Normal AFV at 26 weeks

Oligohydramnios was defined by an amniotic fluid index < 5 cm or maximum vertical pocket < 2 cm. AFV, amniotic fluid volume.

Fontanella at. All Ultrasound Obstret Gynecol 2019 Apr;53(4):520-524

Antenatal intervention

	Stage I (mild LUTO)	Stage II (severe LUTO, with prenatal findings suggestive of preserved fetal renal function)	Stage III (severe LUTO, with prenatal findings suggestive of fetal abnormal renal function)
Amount of amniotic fluid	Normal	Oligohydramnios or anhydramnios	Oligohydramnios, but usually anhydramnios
Echogenicity of fetal kidneys	Normal	Hyperechogenic	Hyperechogenic
Renal cortical cysts	Absent	Absent	Can be present
Renal dysplasia	Absent	Absent	Can be present
Fetal urinary biochemistry	Favorable	Favorable within three consecutive evaluations	Not favorable after three consecutive evaluations
Fetal intervention	Not indicated	Indicated to prevent pulmonary hypoplasia and severe renal impairment	May be indicated to prevent pulmonary hypoplasia but not postnatal renal impairment; further studies are necessary

The disease can progress from Stage I to Stage II and then to Stage III during pregnancy.
LUTO, lower urinary tract obstruction.

FarrugiaMK, BraunMC, Peters CA, Ruano R, Herndon CD(2017)

Report on The Society for Fetal Urology panel discussion on the

selection criteria and intervention for fetal bladder outlet obstruction.

J Pediatr Urol 13:345–351

Antenatal Intervention

Options:

- Vesicoamniotic shunting

- Foetal cystoscopy

Shunt complications:

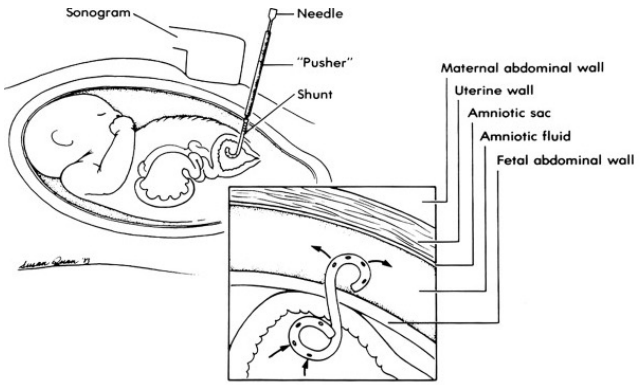
(Nassr et al, 2017, Saccone et al, 2018):

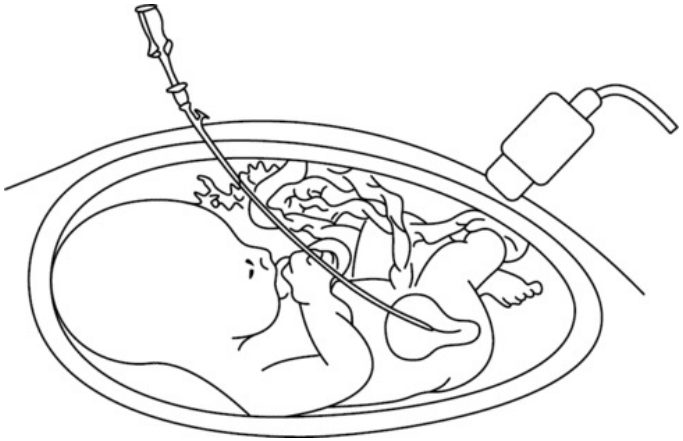
- Blockage or migration 25%
- Preterm delivery – 20%

Foetal cystoscopy complications

(Ruano et al, 2014):

- Urological fistulas – 9%
- Preterm delivery – 20%





Pool question

How many NEW patients with PUV did you see in 2021:

A. 0-1

B. 2-3

C. 4-5

D. More than 5

Postnatal presentation

Age	Non urological	Urological
Neonates	Poor breathing movements, Small chest cavity, respiratory distress due associated pulmonary hypoplasia, urinary ascites, Potter's facies, limb deformities e.g., indentation of knee and elbow due to compression	Poor Stream Palpable bladder Palpable kidneys
Infant	Failure to thrive, vomiting, dehydration, hypotonia, fever, uremia, metabolic acidosis, electrolyte imbalance	Weak stream or dribbling of urine Urosepsis Straining or grunting while voiding
Older boys	Poor growth, hypertension, lethargy, large abdominal mass in suprapubic region	Weak or abnormal urinary stream, Urinary tract infections, Diurnal enuresis (incontinence) in boys older than 5 years, Secondary diurnal enuresis, voiding pain or voiding dysfunction, Urgency, frequency, hesitancy.
Incidental		Incidentally diagnosed hydronephrosis on ultrasound done for unrelated condition, Urinary tract infections, Proteinuria, Increased serum creatinine

J Indian Assoc Pediatr Surg. 2019 Jan-Mar; 24(1): 4–14.

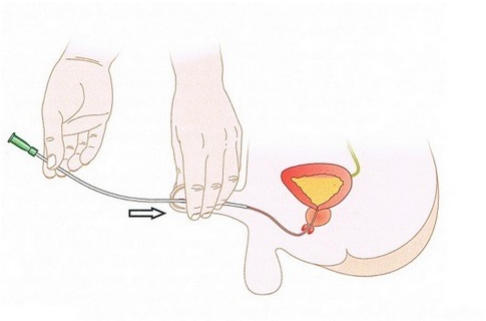
Indications for VCUG in postnatal period in patients with PUV

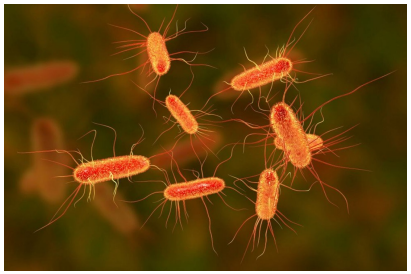
Indication for MCUG	Number of patients	
	< 1 year	*> 1 year*
Antenatal hydronephrosis	27	
UTI	38	11
Renal impairment		3
Incontinence		16
Other		16

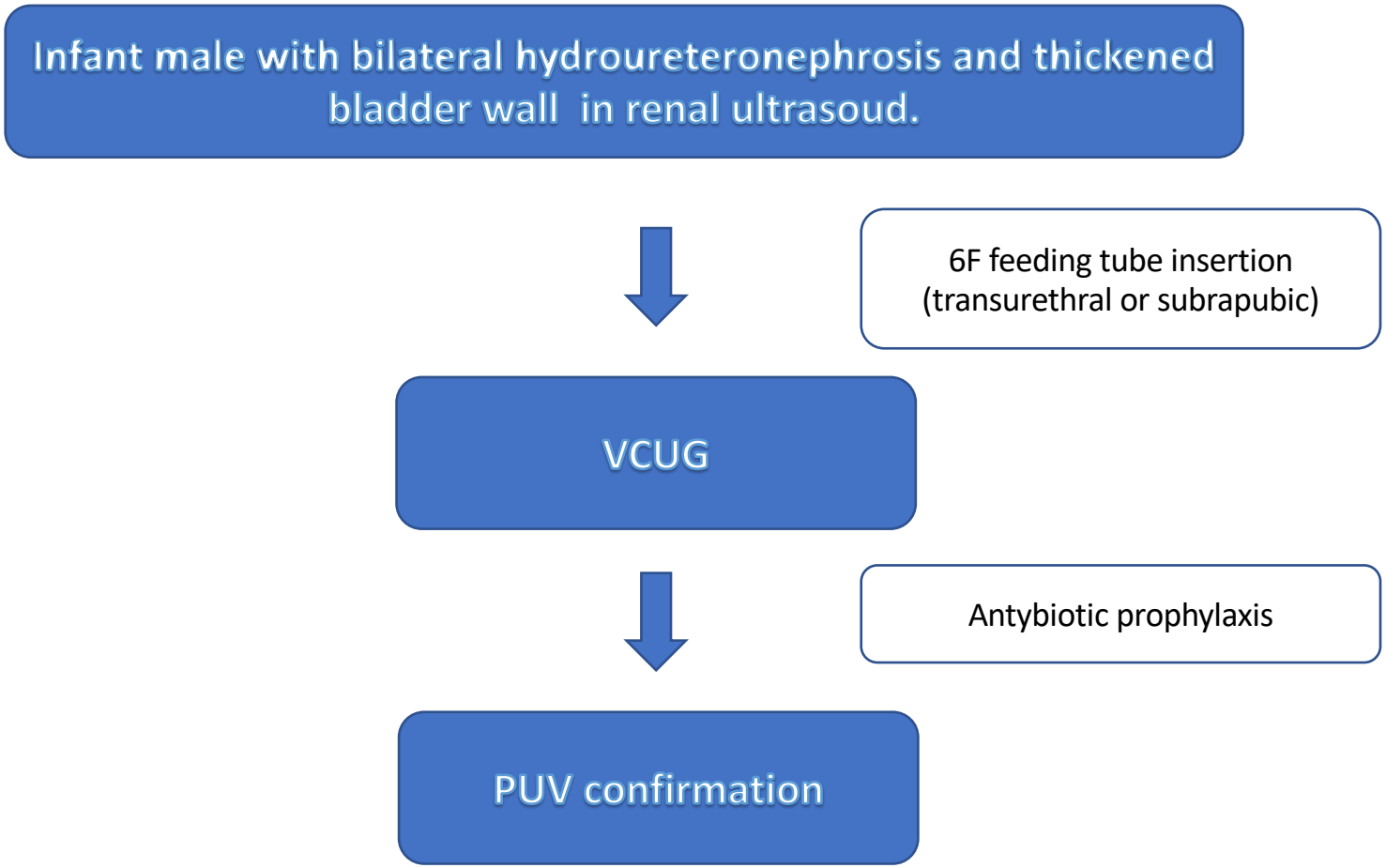
Journal of Pediatric Surgery 54 (2019) 313–317

Postnatal treatment

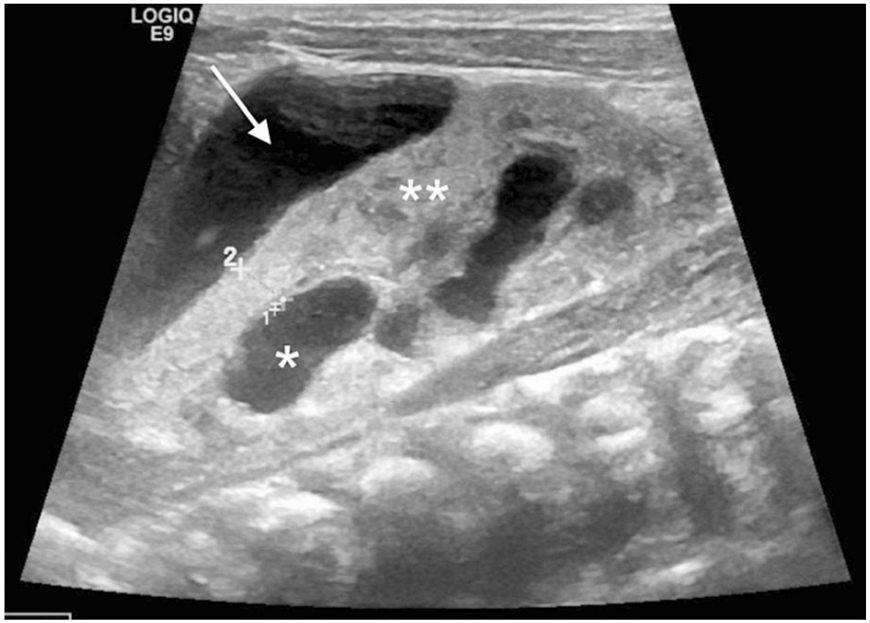
- Bladder drainage through urethral or suprapubic catheter
- Monitoring of serum electrolyte including serum bicarbonate and fluid status is required
- Evaluation of creatinine after 48h reflects neonatal kidney function, (before - mother renal function)
- Treatment of infection if present

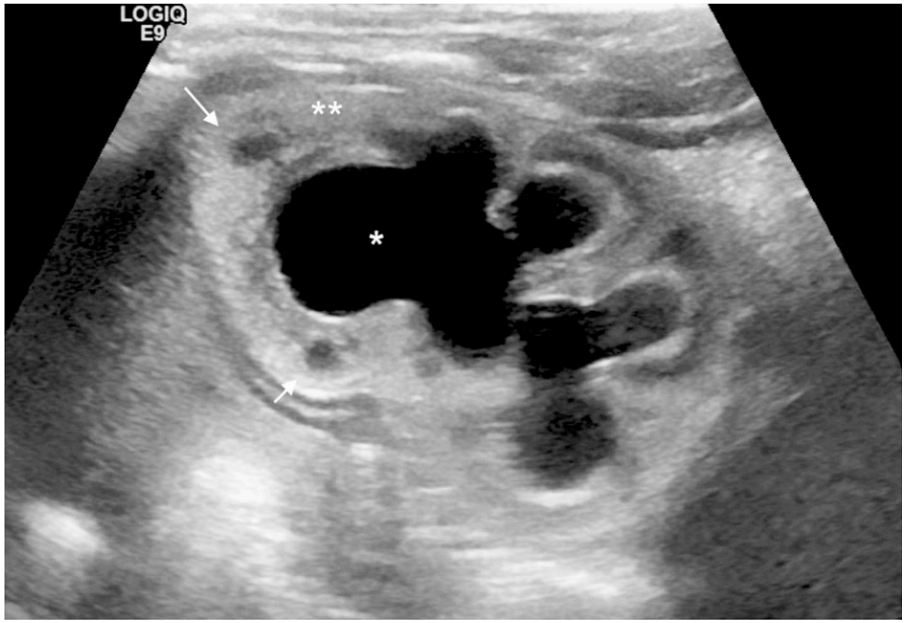




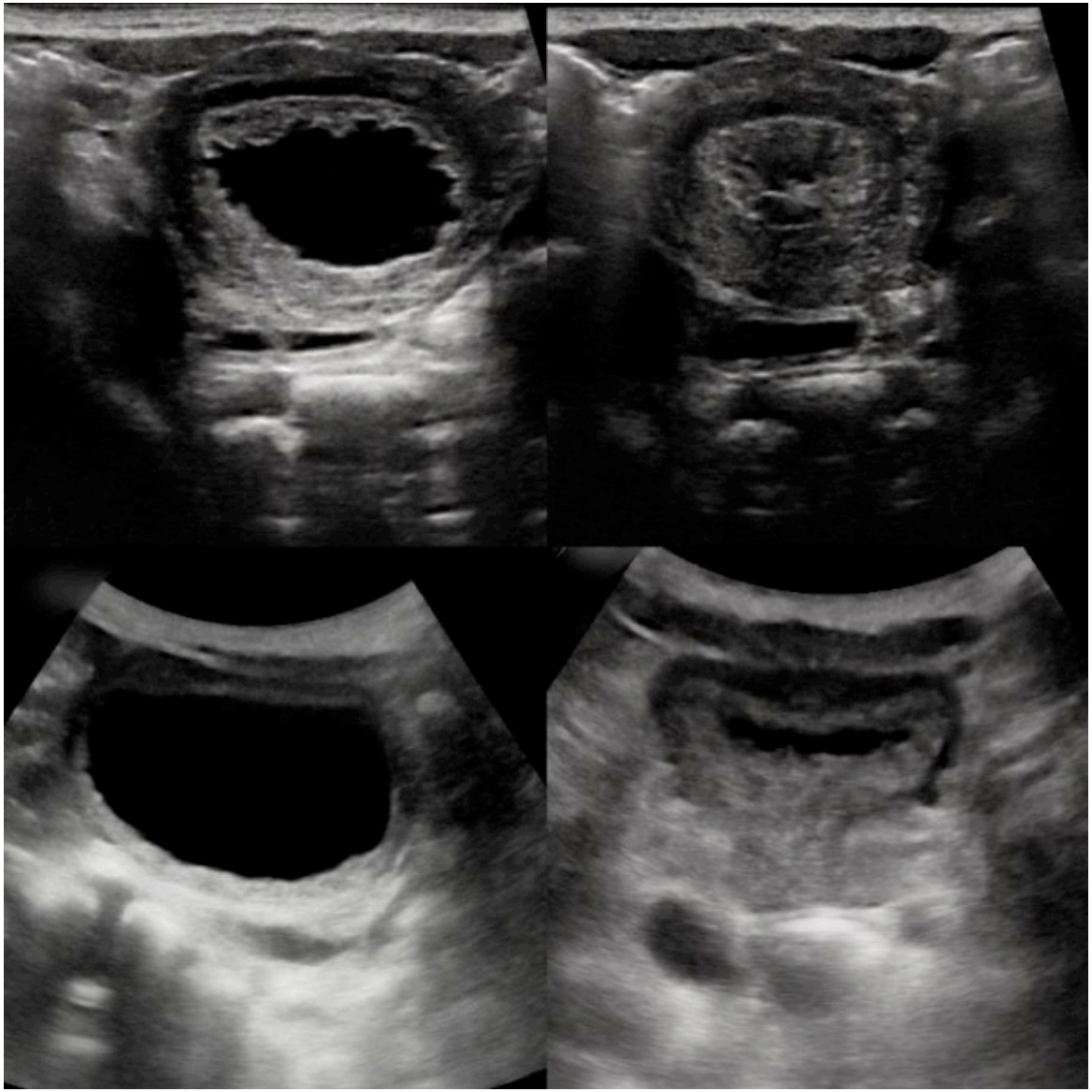

Infant male with bilateral hydroureteronephrosis and thickened bladder wall in renal ultrasoud.
6F feeding tube insertion (transurethral or subrapubic)
VCUG
Antybiotic prophylaxis
PUV confirmation

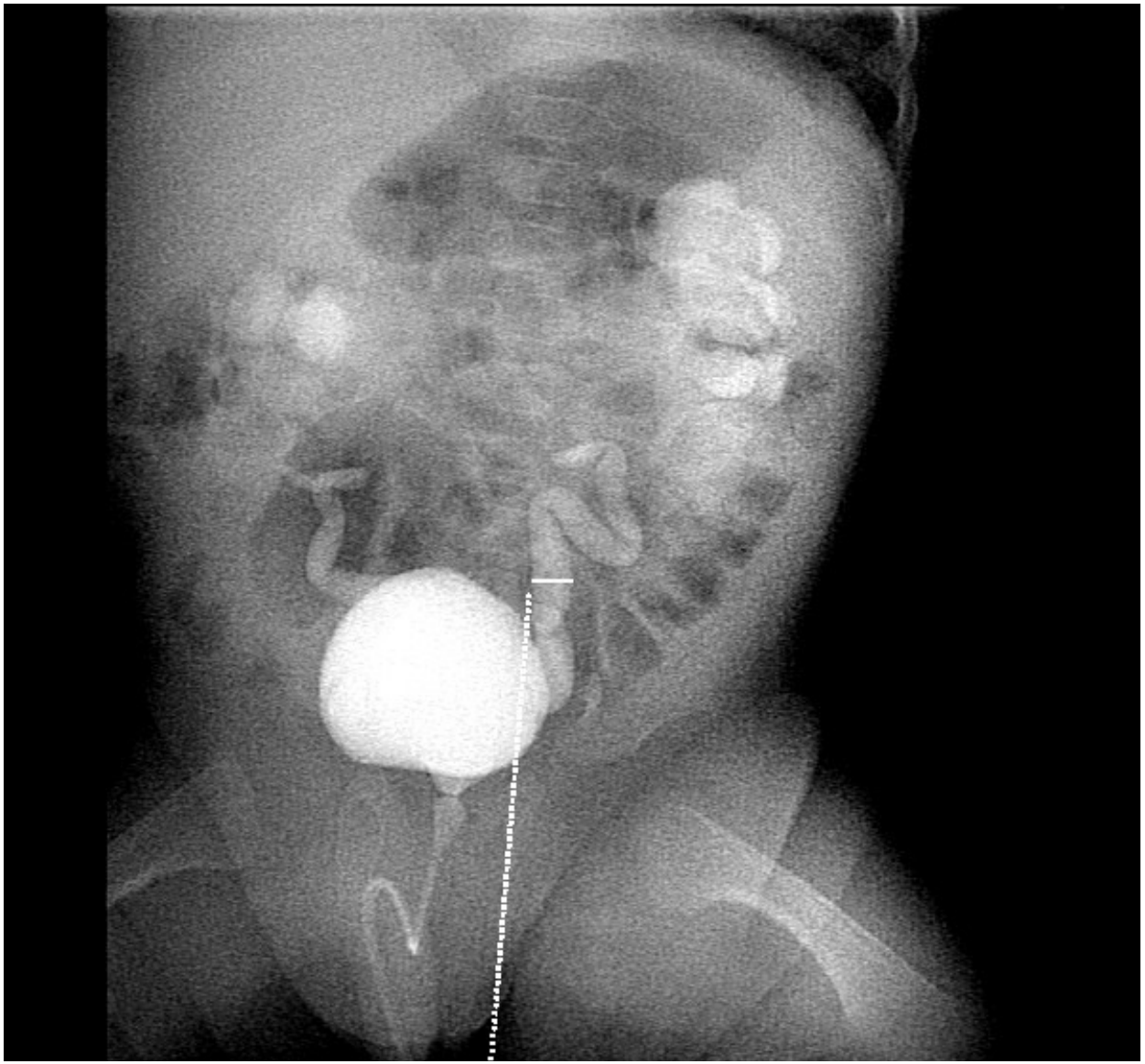
Postnatal presentation - ultrasound





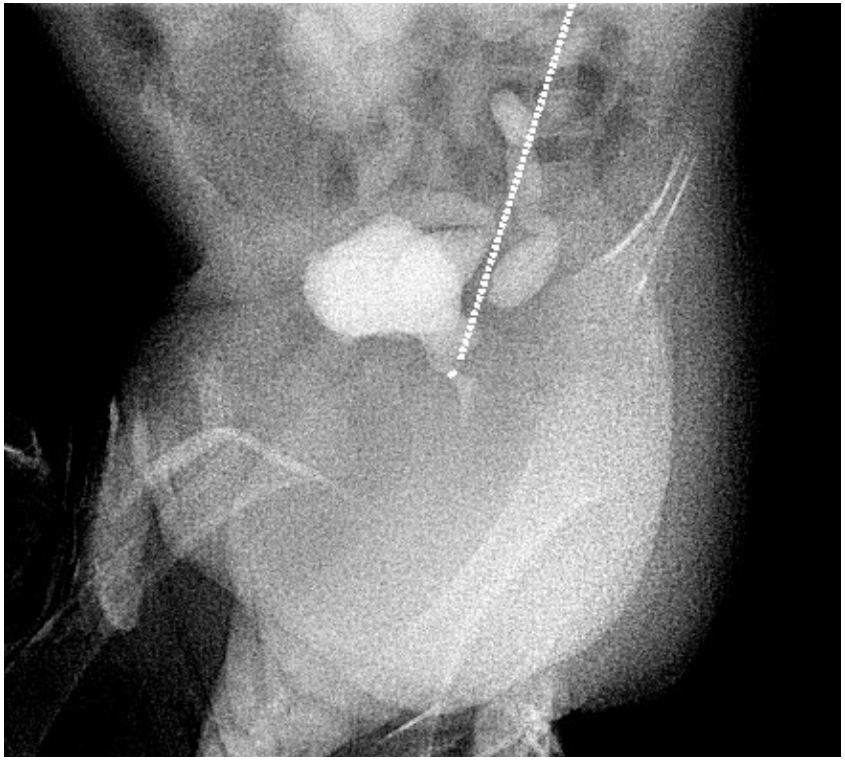
Pediatr Radiol (2016) 46:1418–1423

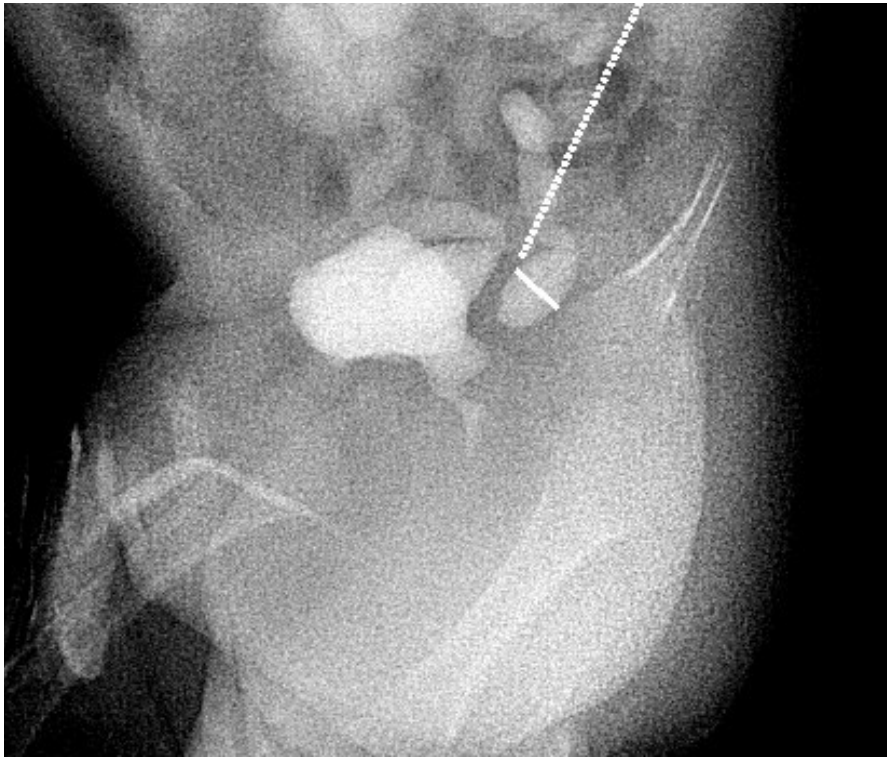




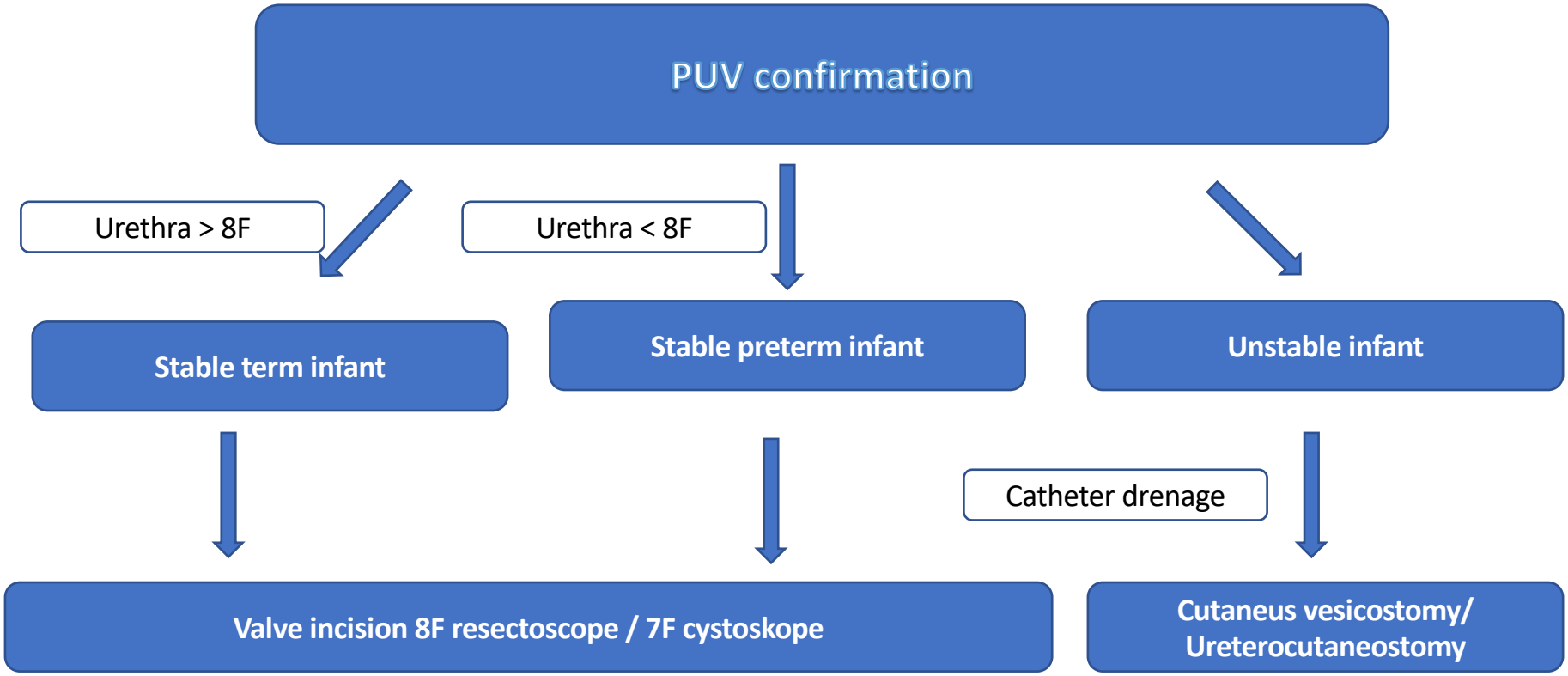
Courtesy Dep. Pediatric Radiology MUG

Postnatal presentation - VCUG





Courtesy Dep. Pediatric Radiology MUG



Consensus on the Management of Posterior Urethral Valves from Antenatal Period to Puberty J Indian Assoc Pediatr Surg. 2019

Table 1
BAPS CASS PUV study initial management and outcome results stratified by presentation: antenatal vs. postnatal vs. late.

	Presentation	Antenatal	Postnatal	Late (>1 y)	p Value
	Patients	45	48	28	
Initial management and response	Catheter	44(98%)	35(73%)	8(29%)	0.0001
	Polyuria (%)	23(51%)	12(25%)	0(0%)	0.0001
	Polyuria (days) Median (Range)	2(0–31)	0(0–24)	0(0)	0.01
	Creatinine Peak (IQR)	136(83–208)	39(25–76)	46(34–60)	0.0001
	Creatinine Plateau	58(43–146)	26(20–40)	45(36–55)	0.0001
	Creatinine 1-month nadir	39(30–72)	26(21–36)	42(34–52)	0.01
Primary surgery	Trans-urethral incision (TUI)	39(87%)	46(95%)	23(82%)	0.1
	Vesicostomy	2(5%)	0	0	
	Ureterostomy	0	0	0	
Secondary surgery	Ureterostomy	1	1	0	
Timing	With TUR	19	8	2	0.01
Circumcision	Delayed	8	12	0	
	Not done	18	28	26	

Journal of Pediatric Surgery 54 (2019) 313–317

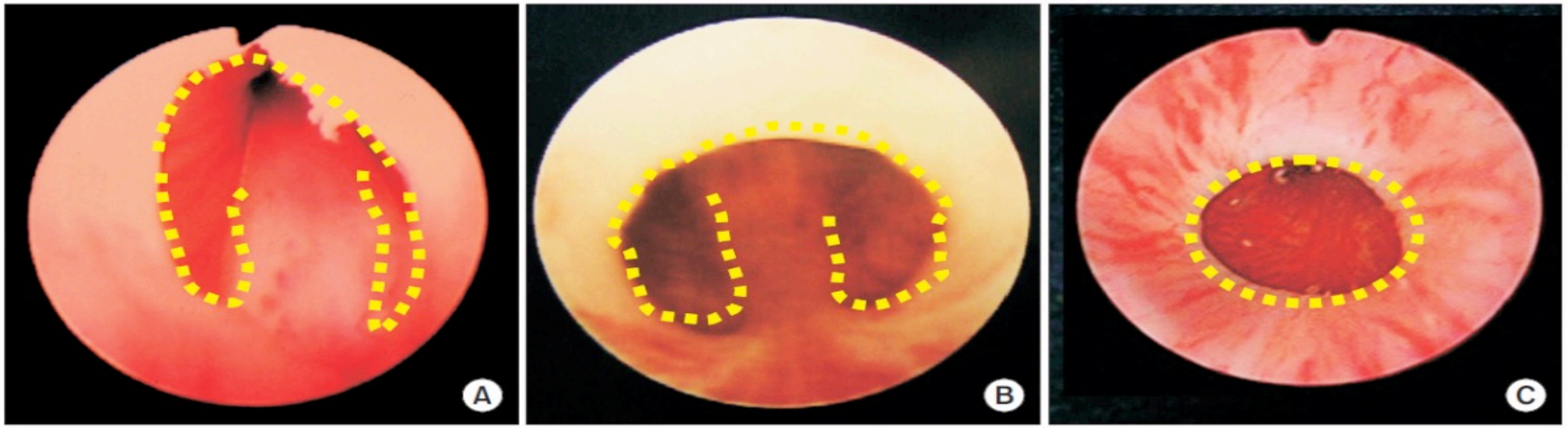


Fig. 4. Endoscopic findings of type 1 posterior urethral valves (PUVs) (A, B) and type 3 PUV (C). Valve like structure (A), membrane like structure (B), and so called "Cobb's collar" seen in type 3 PUV (C). Dotted line depicts margin of the lesion.

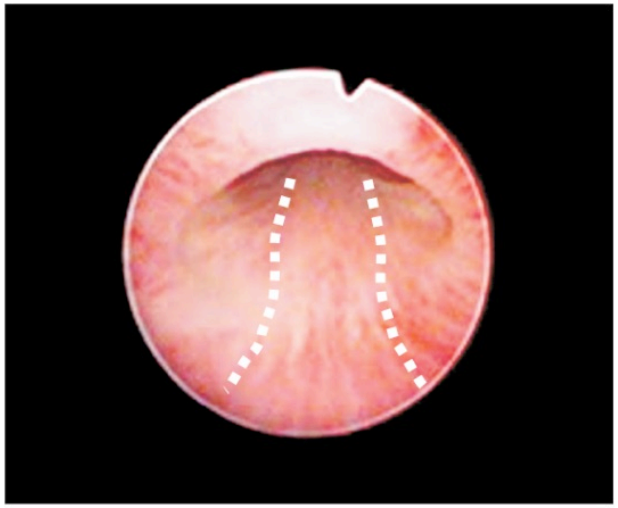
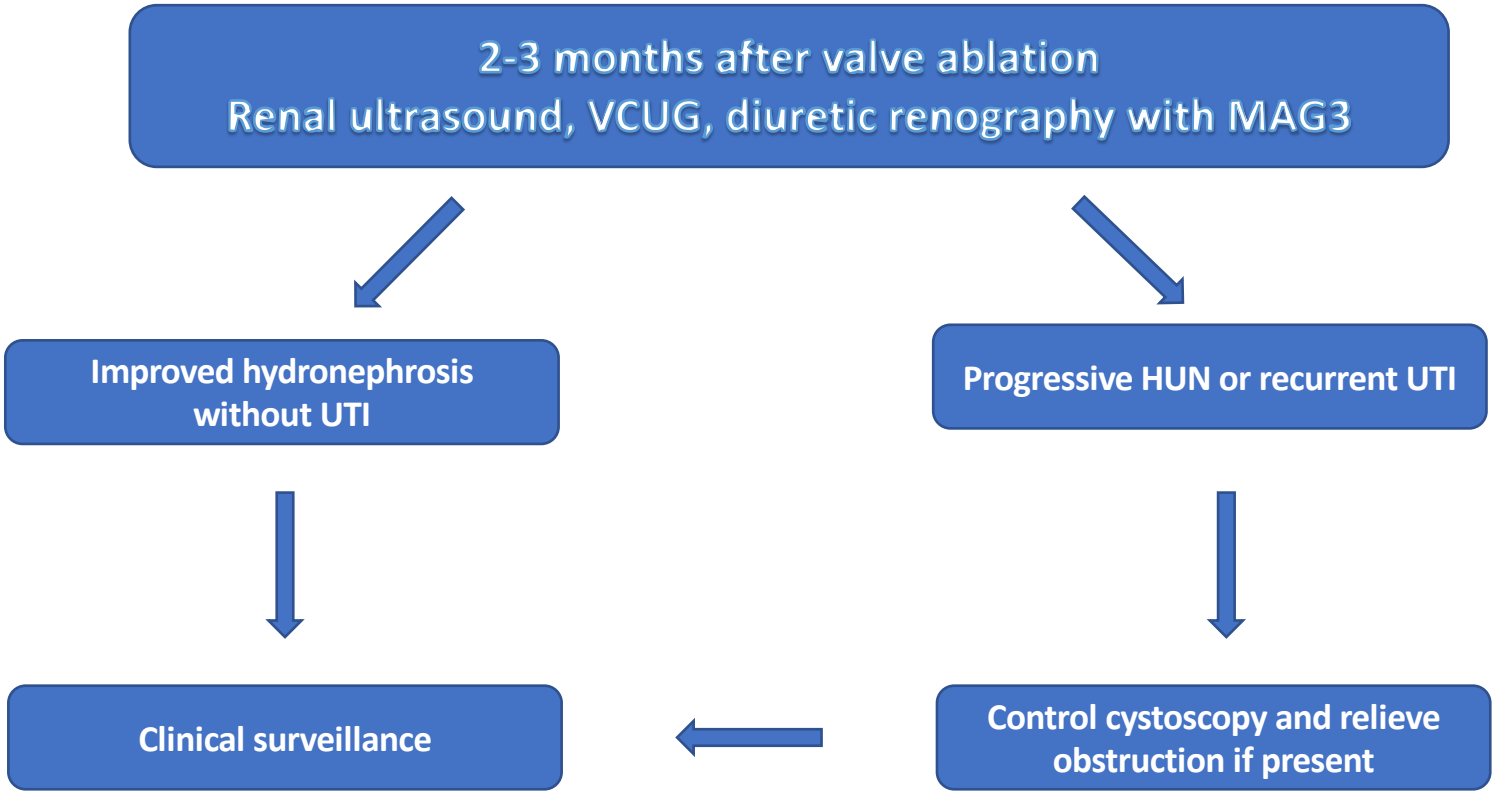


Fig. 5. Normal endoscopic view of membranous urethra in male children. The dotted line shows that distal part connecting to the inferior crest is flat and straight.

Postnatal surgical treatment

- Cystoscopic valve ablation (treatment of choice)
- Vesicostomy – primary valve ablation is associated with better bladder function than vesicostomy (Puri 2002)
- Ureterostomy – temporary high diversion does not have negative influence on bladder function (Ghanem 2005), long term bladder function of patients with PUV treated with temporary supravesical diversion is affected more than those treated with valve ablation alone (Podesta M 2002)


2-3 months after valve ablation
Renal ultrasound, VCUG, diuretic renography with MAG3
Improved hydronephrosis without UTI
Progressive HUN or recurrent UTI
Clinical surveillance
Control cystoscopy and relieve obstruction if present

PUV– after relief

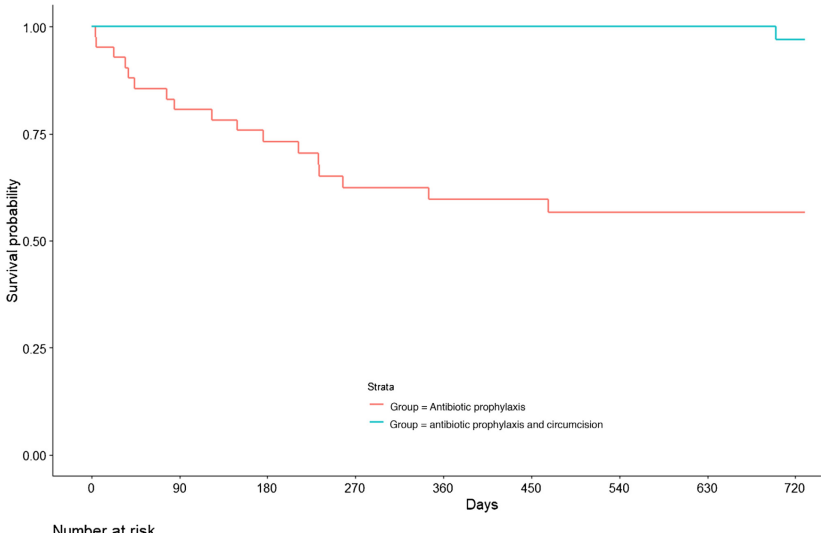
Persistent Upper Urinary Tract Dilatation:

- Residual valve or iatrogenic stricture of the urethra (reevaluation witch VCUG or cystoscopy 2-3 month after primary ablation)
- Vesicoureteral junction obstruction (bladder wall hypertrophy)
- Polyuria (poor concentrating ability or CKD or both)
- Bladder neck hypertrophy
- High post void residuals

UTI and Circumcision

UTI is one of the most common complication – 20 - 40% patients in first year after ablation.

It could be reduced by circumcision to 3%.



Circumcision and Risk of Febrile Urinary Tract Infection in Boys with Posterior Urethral Valves: Result of the CIRCUP Randomized Trial. Eur Urol 2022 Jan;81(1):64-72

Pool question

Which timing of PUV diagnosis is associated with best prognosis for normal kidney function:

A. Antenatally diagnosed

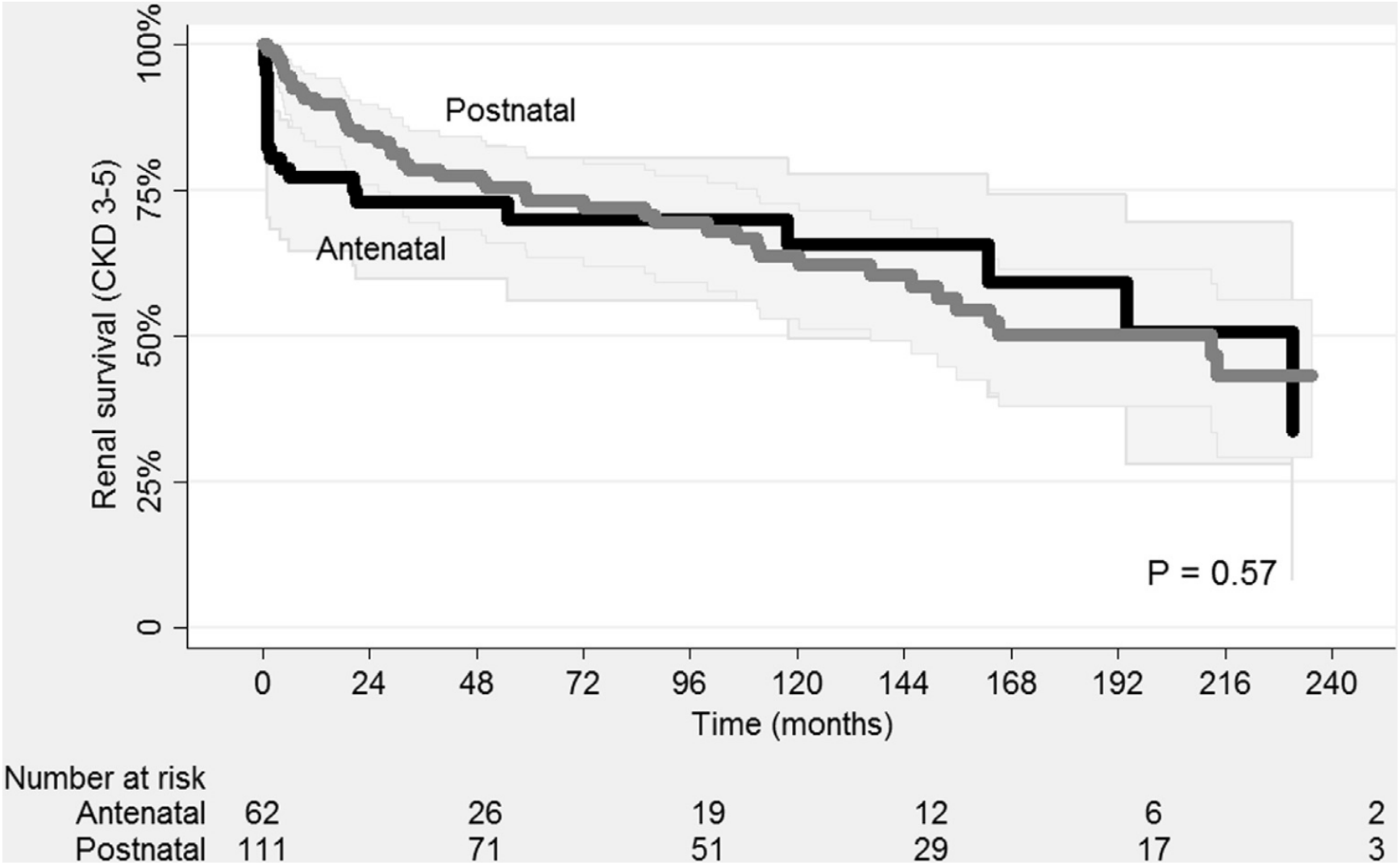
B. Diagnosed during 1 year of life

C. Diagnosed after 1 year of life

D. They have equal prognosis for kidney function

Findings at diagnosis	Antenatal	Postnatal (infancy)	Late (> 1 y)	p Value
Creatinine (μmol/l)*	54 (39.5–109.5)	34 (21–47)		0.0005
Renal units	81	54	40	
APD (mm)*	9.5 (0–19)	5.5 (0–10)	0 (0–9)	0.0001
Hydroureter (mm)*	5 (0–8)	0 (0–7)	0 (0)	0.002
Renal dysplasia	46 (56%)	30 (41%)	8 (20%)	0.0007
Cortical thinning	29 (35%)	21 (28%)	4 (10%)	0.01
Poor CMD	31 (38%)	19 (26%)	4 (10%)	0.005
Cortical cysts	20 (24%)	14 (19%)	0 (0%)	0.003

Ruth Wragg at al.The postnatal management of boys in a national cohort of bladder outlet obstruction,
J Ped Surg (2019),Vol 54,Issue 2, 313-317,



Vasconcelos MA, Journal of Pediatric Urology (2019) 15, 167.e1-e8

PUV metabolic consequences

Significant post-obstructive diuresis related to medullary damage (Li C 2001)

Transient severe hyponatremia – need for sodium supplementation (Bulchmann G 2001, Venglarcik JS 1981)

Long term renal tubular acidosis up to 20% of patients with PUV and normal eGFR. (Sharma AP 2001, 2009)

Table 1
BAPS CASS PUV study initial management and outcome results stratified by presentation: antenatal vs. postnatal vs. late.

	Presentation	Antenatal	Postnatal	Late (>1 y)	p Value
	Patients	45	48	28	
Initial management and response	Catheter	44(98%)	35(73%)	8(29%)	0.0001
	Polyuria (%)	23(51%)	12(25%)	0(0%)	0.0001
	Polyuria (days) Median (Range)	2(0–31)	0(0–24)	0(0)	0.01
	Creatinine Peak (IQR)	136(83–208)	39(25–76)	46(34–60)	0.0001
	Creatinine Plateau	58(43–146)	26(20–40)	45(36–55)	0.0001
	Creatinine 1-month nadir	39(30–72)	26(21–36)	42(34–52)	0.01
Primary surgery	Trans-urethral incision (TUI)	39(87%)	46(95%)	23(82%)	0.1
	Vesicostomy	2(5%)	0	0	
	Ureterostomy	0	0	0	
Secondary surgery	Ureterostomy	1	1	0	
Timing	With TUR	19	8	2	0.01
Circumcision	Delayed	8	12	0	
	Not done	18	28	26	

PUV and hypertension

Incidence of hypertension in PUV patients:

9% (Parkhouse 1988),

13% (Lopez Pereira 2013),

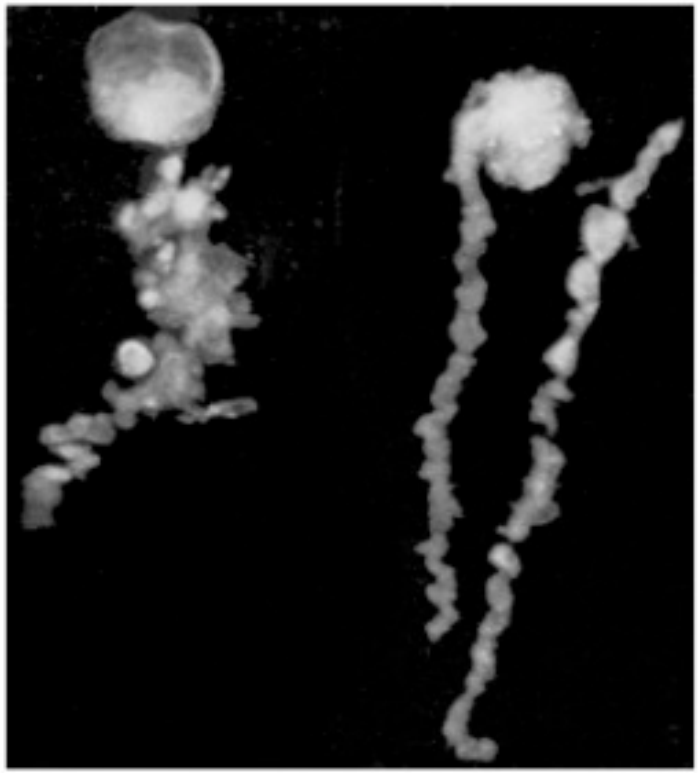
21% (Vasconcelos 2019),

56% (Heikkila 2020)

Increase of PRA level (Heikkila 2020)

Atubular glomeruli theory

(Chevalier 2008)



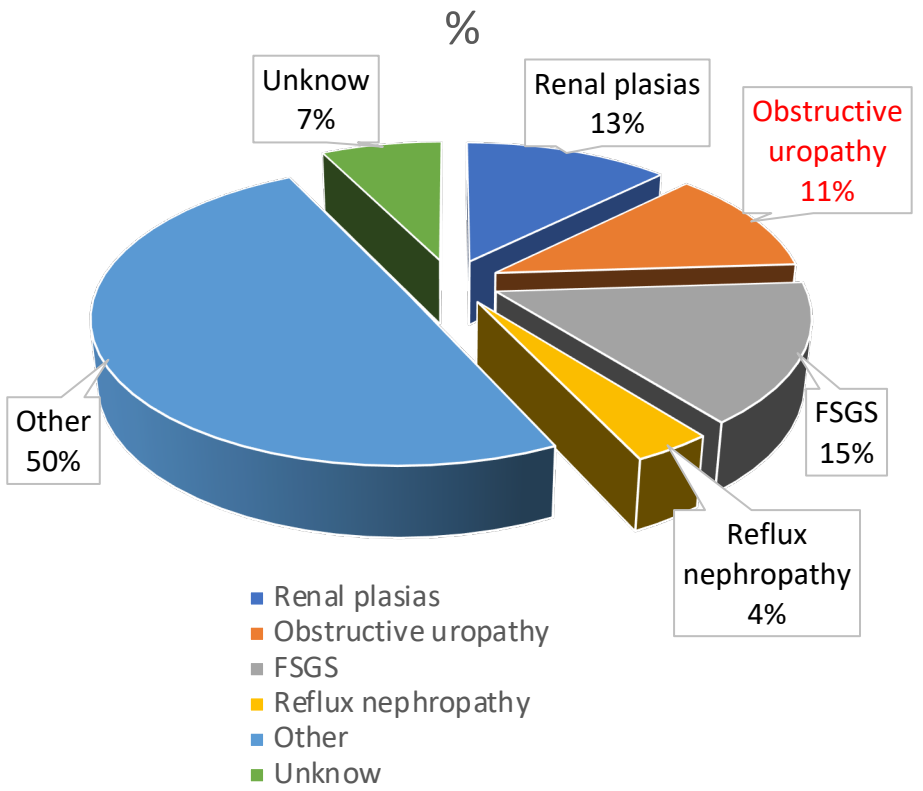
Chevalier RL, Forbes MS. Generation and evolution of atubular glomeruli in the progression of renal disorders. *J Am Soc Nephrol.* 2008;19:197–206.

Chevalier RL, Thornhill BA, Forbes MS, Kiley SC. Mechanisms of renal injury and progression of renal disease in congenital obstructive nephropathy. *Review. Pediatr Nephrol.* 2010;25:687–697.

Konda R, Orikasa S, Sakai K, Ota S, Kimura N. The distribution of renin containing cells in scarred kidneys. *J Urol.* 1996;156:1450–1454.

PUV - kidney function consequences

Up to 11% of paediatric ESRD and initiating dialysis is contributed by PUV during the period 2002-2011 (NAPRTCS Raport).



Weaver, D.J., Somers, M.J.G., Martz, K. *et al.* Clinical outcomes and survival in pediatric patients initiating chronic dialysis: a report of the NAPRTCS registry. *Pediatr Nephrol* **32,** 2319–2330 (2017)

Pool question

What is the cumulative risk of ESRD in patients with PUV, when they reach adulthood:

A. 10%

B. 25%

C. 50%

D. 75%

PUV - kidney function consequences

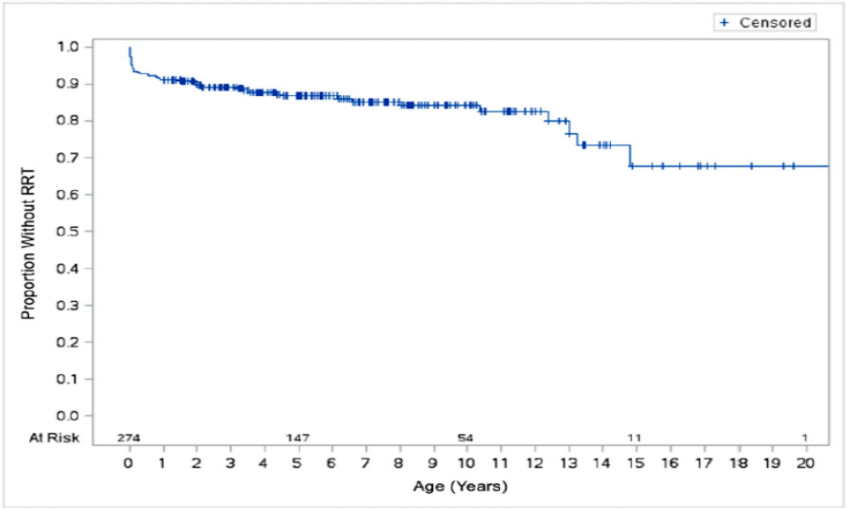
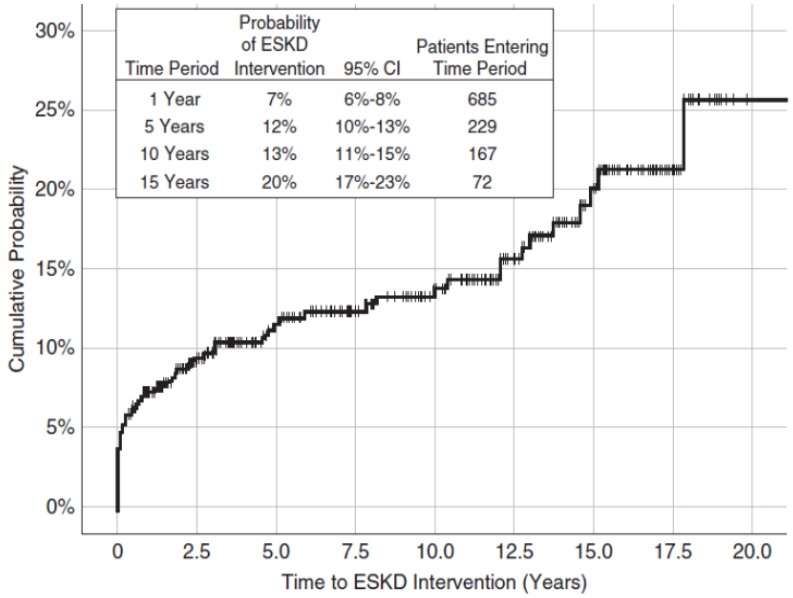


FIGURE 1
Kaplan-Meier estimates of age at RRT (PUV cohort; 1995–2015).



McLeod at al. Renal replacement therapy and CIC risk in PUV patients Pediatrics (2019),143(3)

Herbst KW at al. Survival and Kidney Outcomes of Children with an Early Diagnosis of Posterior Urethral Valves Clin J Am Soc Nephrol (2019) 7:14(11):1572-1580

Prognostic markers of CKD/ESRD

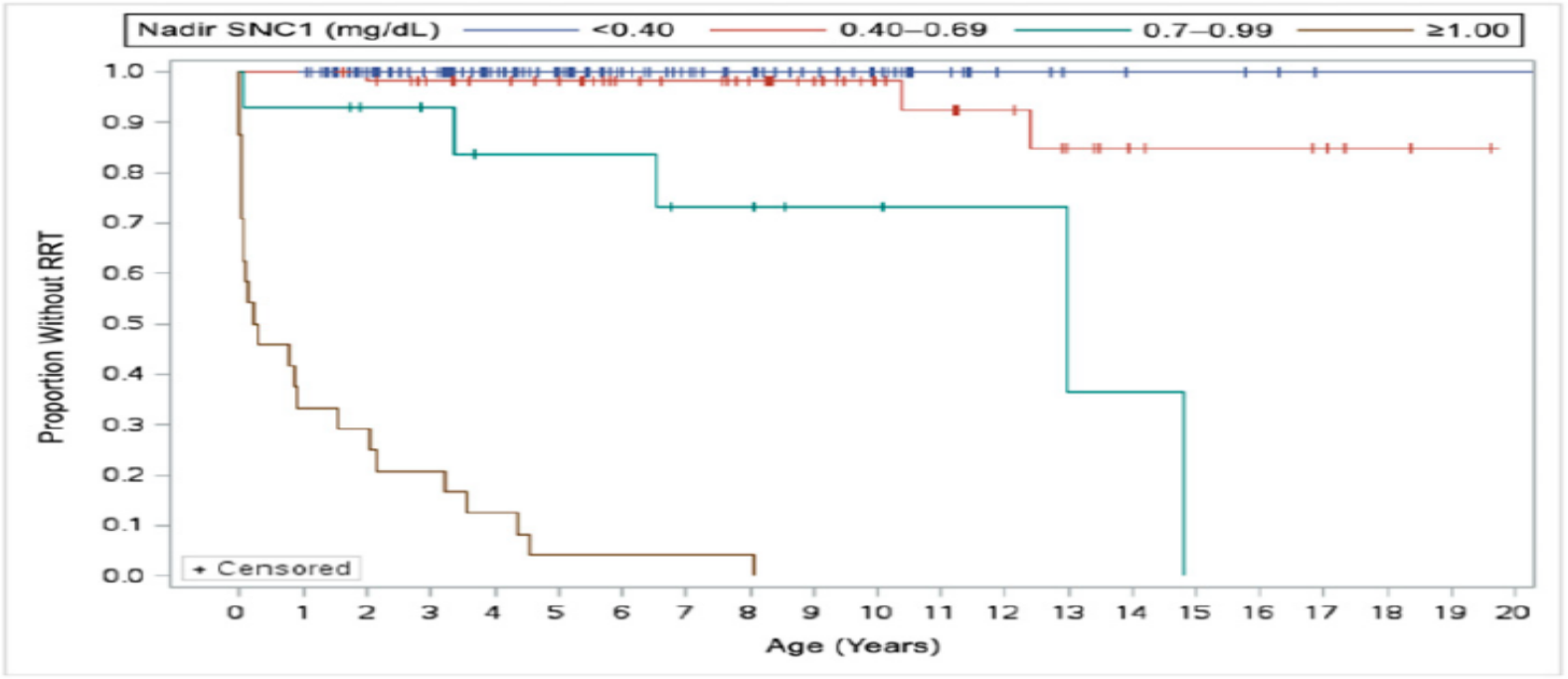


FIGURE 2
Kaplan-Meier estimates of age at RRT, stratified by SNC1 (PUV cohort; 1995–2015).

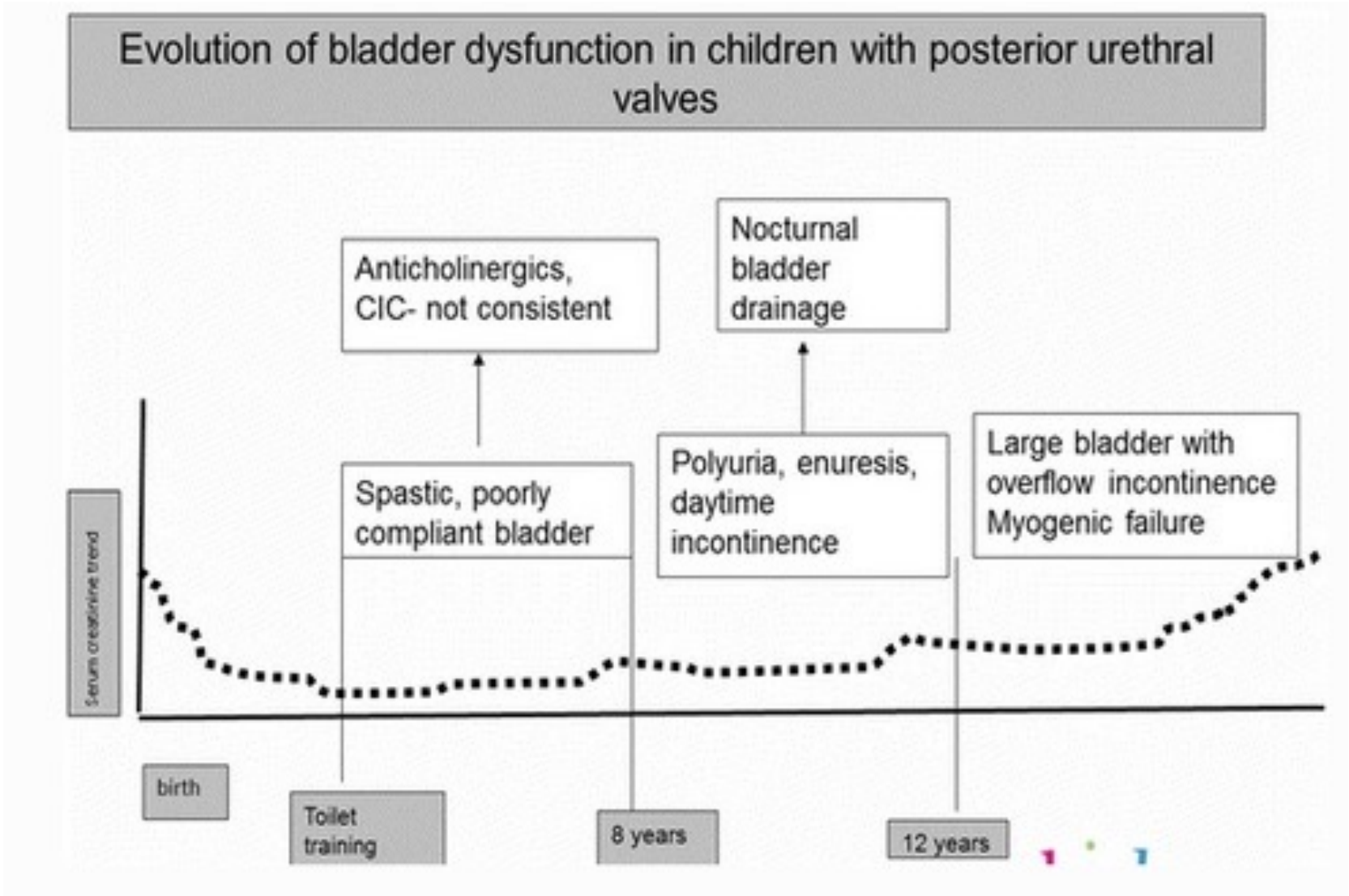
To cite: McLeod DJ, Szymanski KM, Gong E, et al. Renal Replacement Therapy and Intermittent Catheterization Risk in Posterior Urethral Valves. *Pediatrics*. 2019;143(3): e20182656

Prognostic markers of CKD/ESRD

Renal dysplasia features:

- Decreased corticomedullary differentiation predict stage 5 CKD by age of 5 years (Odeh R 2016)
- Renal parenchymal area less than 12,4cm2 in the first postnatal ultrasound is predictive of ESRD in childhood (Pulido JE 2014)

Present LUTS (lower urinary tract dysfunction) – increase risk of developing ESKD or CKD fourfold (RR 4,22 95% CI1,44-12,43 p=0,009) (Deshpande AV 2018)



Deshpande, A.V. Current strategies to predict and manage sequelae of posterior urethral valves in children. *Pediatr Nephrol* **33,** 1651–1661 (2018)

PUV bladder evaluation

Neurourology and Urodynamics

The Standardization of Terminology of Lower Urinary Tract Function in Children and Adolescents: Update Report From the Standardization Committee of the International Children's Continence Society

Paul F. Austin,[1*] Stuart B. Bauer,[2] Wendy Bower,[3] Janet Chase,[4] Israel Franco,[5] Piet Hoebeke,[6] Søren Rittig,[3] Johan Vande Walle,[6] Alexander von Gontard,[7] Anne Wright,[8] Stephen S. Yang,[9,10] and Tryggve Nevéus[11]

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[5]*New York Medical College, Valhalla, New York*
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[7]*Department of Child and Adolescent Psychiatry, Saarland University Hospital, Germany*
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[10]*School of Medicine, Buddhist Tzu Chi University, Hualien, Taiwan*
[11]*Department of Womens and Childrens Health, Section of Paediatric Nephrology, Uppsala University, Uppsala, Sweden*

PUV bladder evaluation

4h bladder observation

(infants and children without bladder control)

higher number of voids, smaller voided volume, higher residual volume (Holmdhal 1998)

Dzień	Godzina	Ilość moczu oddanego na porcję (ml)	Godzina
dzień 1	16:28	X	
	16:43	68	
12.12.21r.	16:58	X	
	17:17	X	
	17:33	X	
	17:49	X	
	18:03	40	
	18:10	X	
	18:37	X	
	18:52	X	
	19:10	24	
	19:26	X	
	19:42	X	
	19:58	X	
~~dzień 2~~	20:14	X	
	20:30	24	

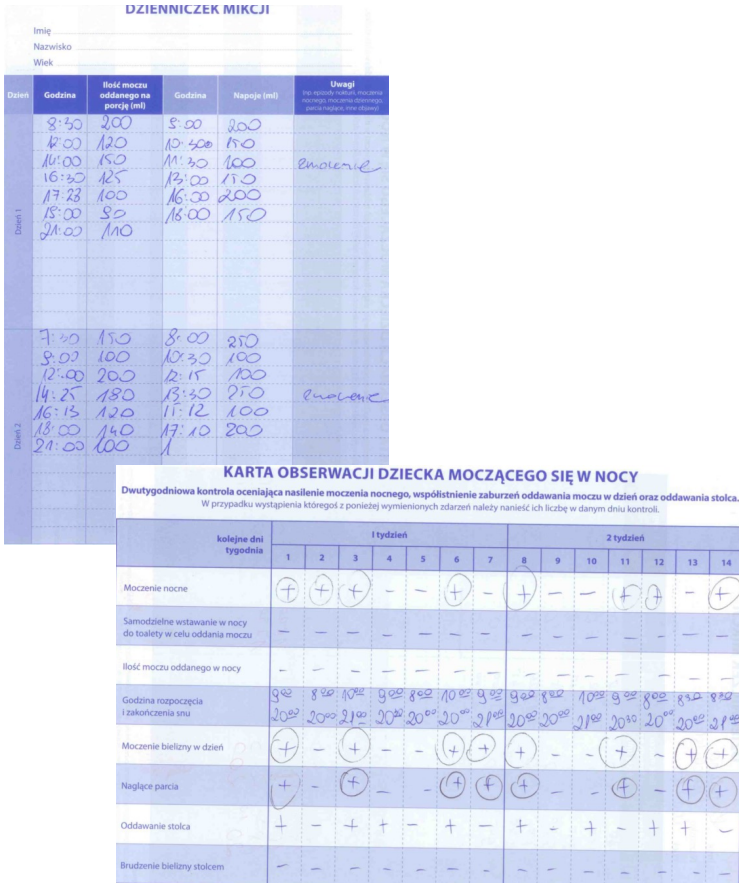
PUV bladder evaluation

48h Frequency/Volume chart

(MVV, voiding frequency and total urine volume)

14 days bladder diary

(frequency of incontinence episodes during the day, urgency symptoms and enuresis episodes)



DZIENNICZEK MIKCJI

Imię
Nazwisko
Wiek

Dzień	Godzina	Ilość moczu oddanego na porcję (ml)	Godzina	Napoje (ml)	Uwagi (np. epizody nietrzymania moczu, moczenia nocnego, moczenia dziennego, parcia naglące, inne objawy)
Dzień 1	8:30	200	5:00	200	
	12:00	120	10:40	150	
	14:00	150	11:30	100	enuresis
	16:30	125	13:00	150	
	17:23	100	16:00	200	
	18:00	80	18:00	150	
	21:00	110			
Dzień 2	7:30	150	8:00	250	
	9:00	100	10:30	100	
	12:00	200	12:15	100	
	14:25	180	13:30	250	enuresis
	16:15	120	11:12	100	
	18:00	140	17:10	200	
	21:00	100	1		

KARTA OBSERWACJI DZIECKA MOCZĄCEGO SIĘ W NOCY

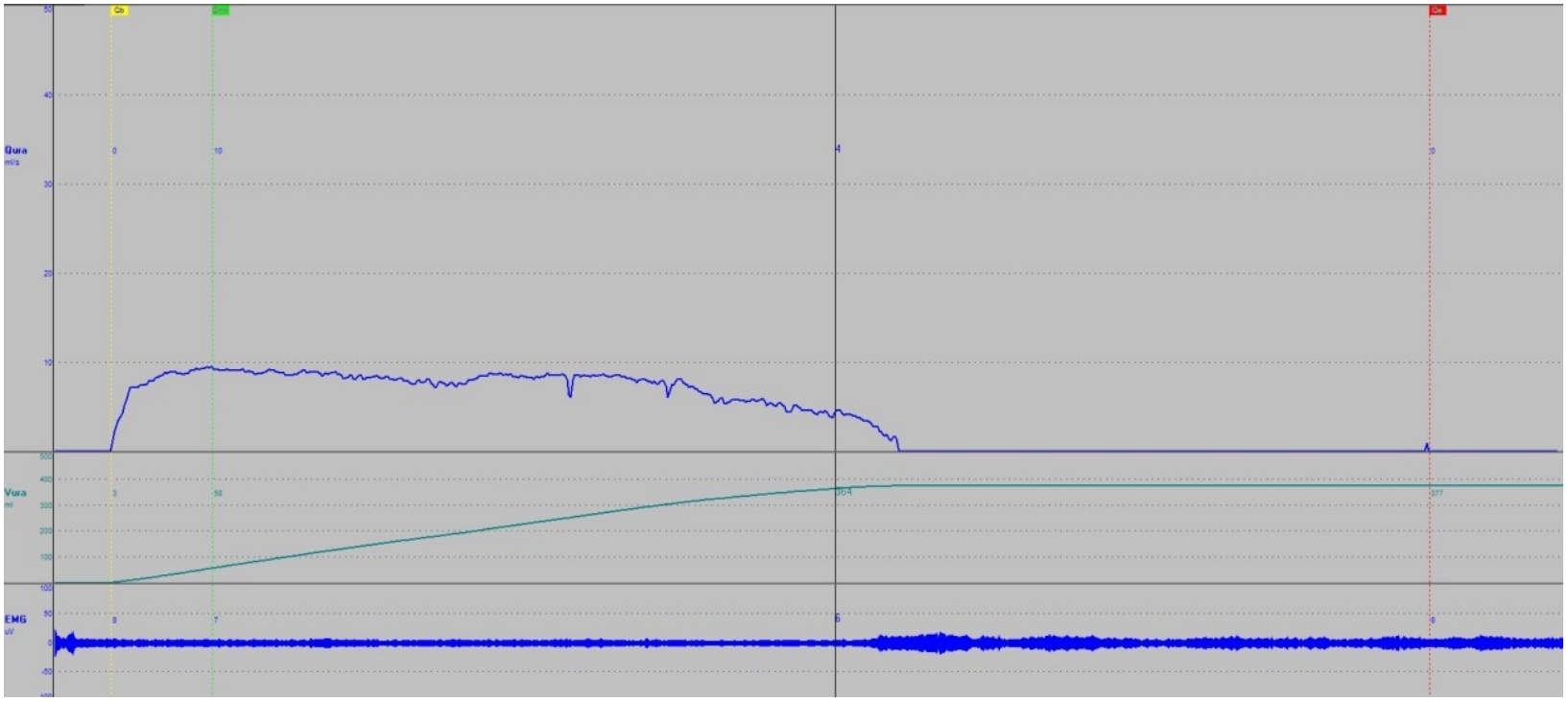
Dwutygodniowa kontrola oceniająca nasilenie moczenia nocnego, współistnienie zaburzeń oddawania moczu w dzień oraz oddawania stolca.
W przypadku wystąpienia któregoś z poniżej wymienionych zdarzeń należy nanieść ich liczbę w danym dniu kontroli.

kolejne dni tygodnia	I tydzień							2 tydzień						
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Moczenie nocne	+	+	+	-	-	+	-	+	-	-	+	+	-	+
Samodzielne wstawanie w nocy do toalety w celu oddania moczu	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ilość moczu oddanego w nocy	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Godzina rozpoczęcia i zakończenia snu	9:00 20:00	8:00 20:00	10:00 21:00	9:00 20:00	8:00 20:00	10:00 20:00	9:00 21:00	9:00 20:00	8:00 20:00	10:00 21:00	9:00 20:00	8:00 20:00	8:00 20:00	8:00 21:00
Moczenie bielizny w dzień	+	-	+	-	-	+	+	+	-	-	+	-	+	+
Naglące parcia	+	-	+	-	-	+	+	+	-	-	+	-	+	+
Oddawanie stolca	+	-	+	+	-	+	-	+	-	+	-	+	+	-
Brudzenie bielizny stolcem	-	-	-	-	-	-	-	-	-	-	-	-	-	-

PUV bladder evaluation

Uroflowmetry with post void residual evaluation with ultrasound

(Curve shape, Qmax, PVR)

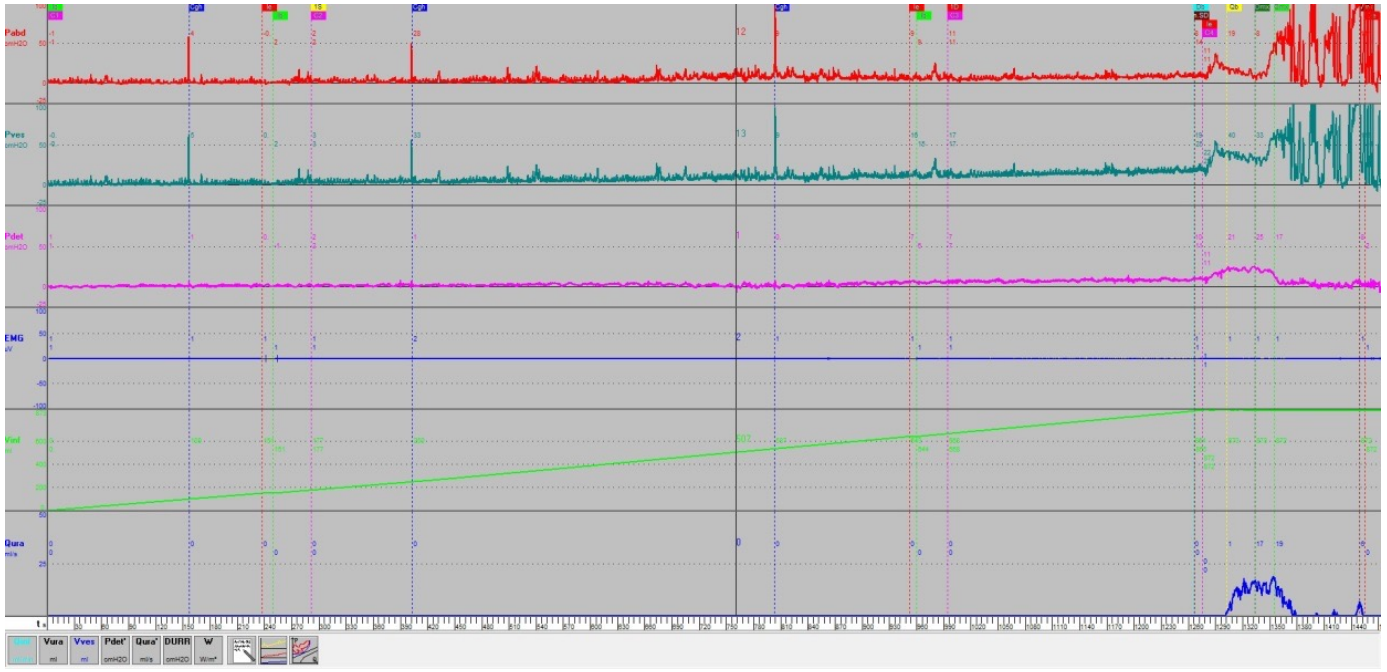


PUV bladder evaluation

Urodynamics

invasive study (filling and voiding phase)

type of bladder dysfunction (decreased compliance, detrusor overactivity, myogenic failure)



Pharmacological Treatment	Indication	Side effects	Comments
Antycholonergic (oxybutynin, solifenacin)	Low compliance bladder, bladder overactivity	Constipation, dry month, blurred vision,	Risk of myogenic failure
Alfa-blockers (doxazosin, terazosin, tamsulosin) off label	Persistent bladder neck hypertrophy, high post-void residuals, myodenic failure, hesitancy	Postural hypotension	Risk of increased incontinence
Desmopressin	Polyuria, nightime bladder overdistension	Hyponatremia (rare)	

Pediatr Nephrol (2018) 33:1651-1661
Eur Urol (2015) 5: 819-825

Mode of treatment	Indications	Side effects	Comments
Urotherapy (proper fluid intake, timed voiding – every 2-3 hours, double voiding)	High capacity bladder, post void residual, daytime incontinence		Suboptimal response due to decreased bladder feeling
Nocturnal drainage using urethral catheter	Overdistension of the bladder with upper tract dilatation	UTI, Low compliance, Low adherence	Mitroffanof procedure (cathaterezable channel) may be helpful
Clean intermittent catheterization	Ineffective bladder emptying, recurrent UTI due to PVR	Trauma (persistent sensation of urethra), low compliance, low adherence	Mitroffanof procedure,
Bladder augmentation	Small, low compliance bladder, high storage pressure despite all therapy	UTI, stones, metabolic changes, low risk of malignancy in long term	Not commonly needed in children without ESRD

Pediatr Nephrol (2018) 33:1651-1661

Risk of CIC

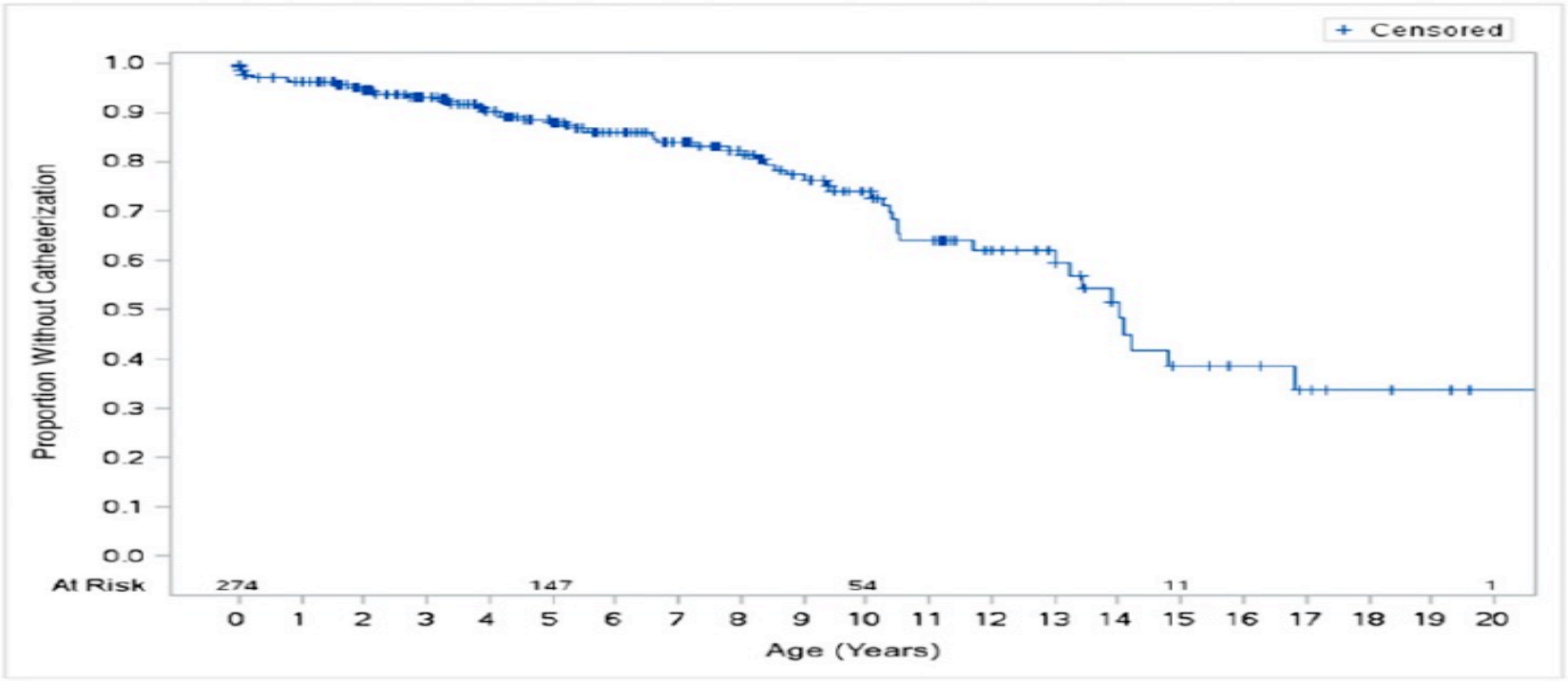


FIGURE 3
Kaplan-Meier estimates of age at recommendation for CIC (PUV cohort; 1995–2015).

To cite: McLeod DJ, Szymanski KM, Gong E, et al. Renal Replacement Therapy and Intermittent Catheterization Risk in Posterior Urethral Valves. *Pediatrics*. 2019;143(3): e20182656

Late PUV presentation

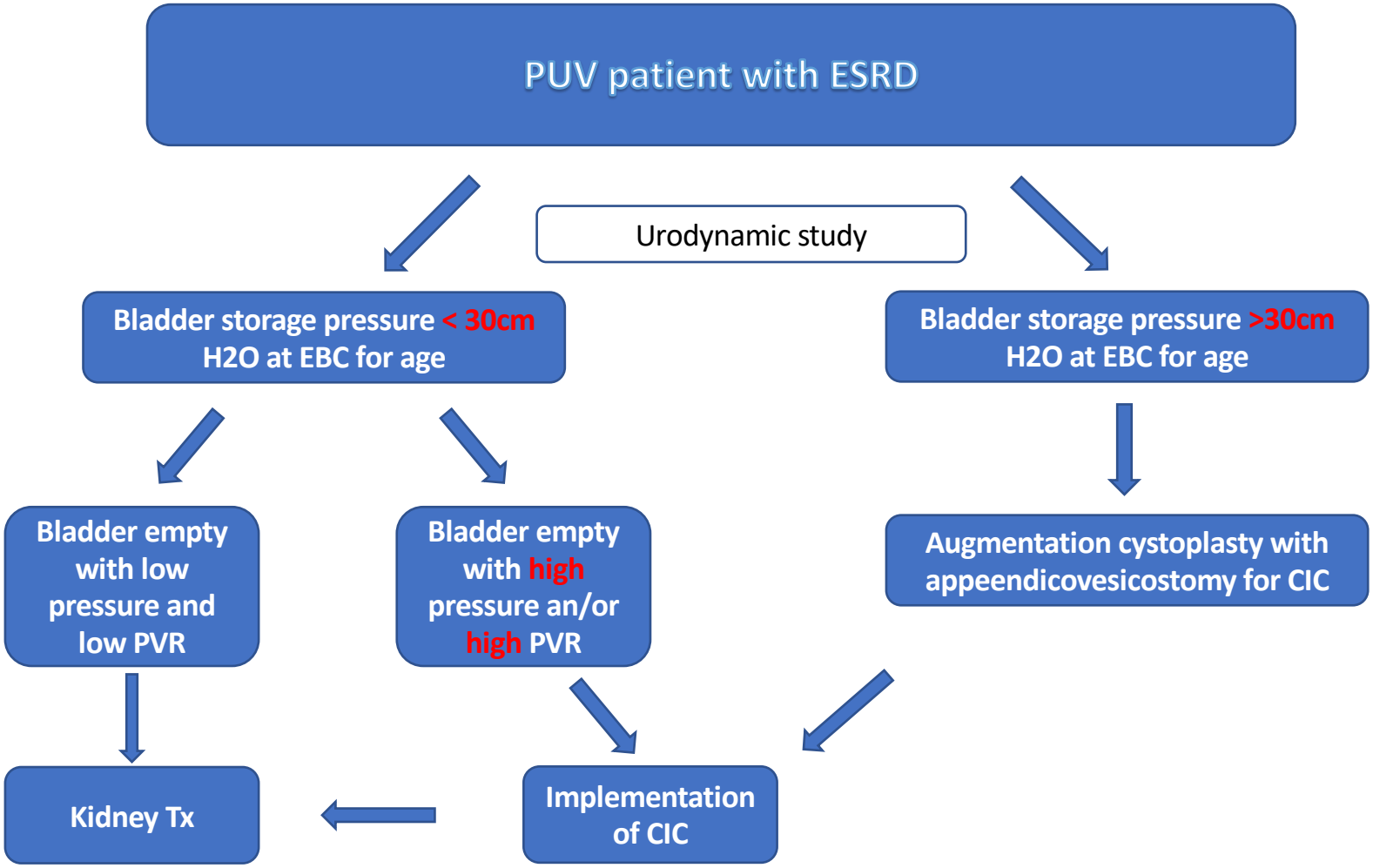
When to suspect late PUV:

- Obstructive pattern in uroflow with EMG, (excluding voiding dysfunction) or in urodynamics (suprapubic catheter may be needed)
- OAB in boys refractory to urotherapy and cholinolytics
- High Pdet max in urodynamics
- Persistent VUR in older boys

World J Urol (2019) 37(9): 1973-1979

Most patients with recognized late PUV have normal imaging of the urinary tract, but presented night time incontinence and frequency. BJU Int 94(4): 616–619.

Cystourethroscopy examination should be preferred to diagnose posteriori urethral valves regardless of VCUG results. Eur J Pediatr Surg. 2019;29(1):85–89.


PUV patient with ESRD
Urodynamic study
Bladder storage pressure < 30cm H2O at EBC for age
Bladder storage pressure >30cm H2O at EBC for age
Bladder empty with low pressure and low PVR
Bladder empty with high pressure an/or high PVR
Augmentation cystoplasty with appeendicovesicostomy for CIC
Kidney Tx
Implementation of CIC

Transplantation in PUV patients

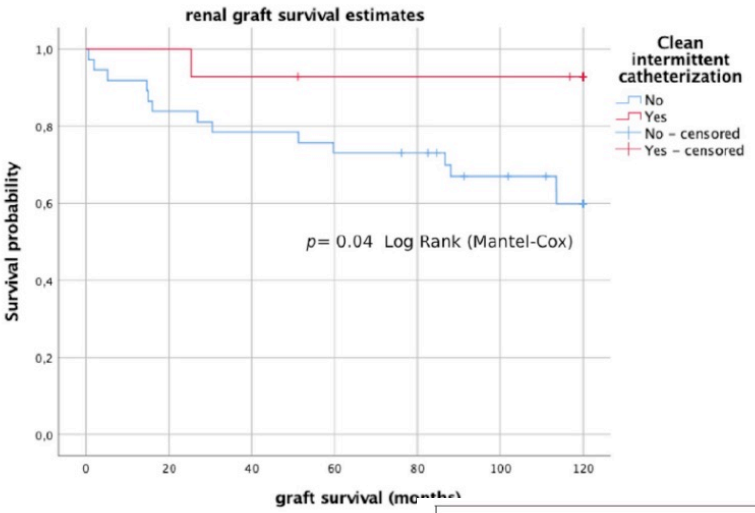


FIGURE 1 | Long-term graft survival (Kaplan–Meier analysis) in patients with CIC and witl

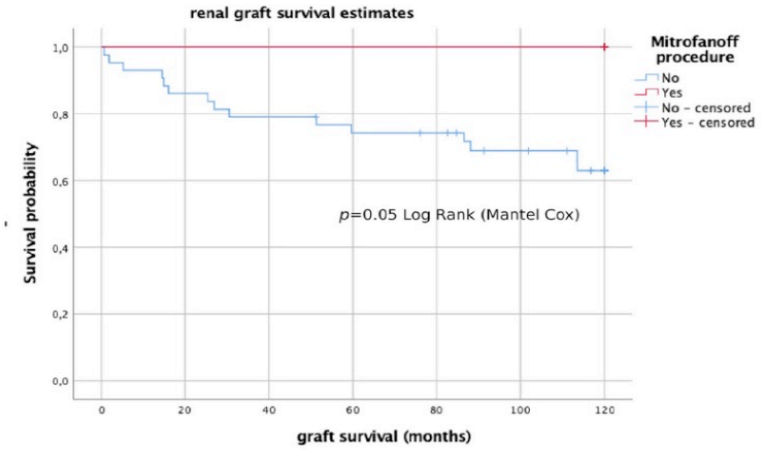
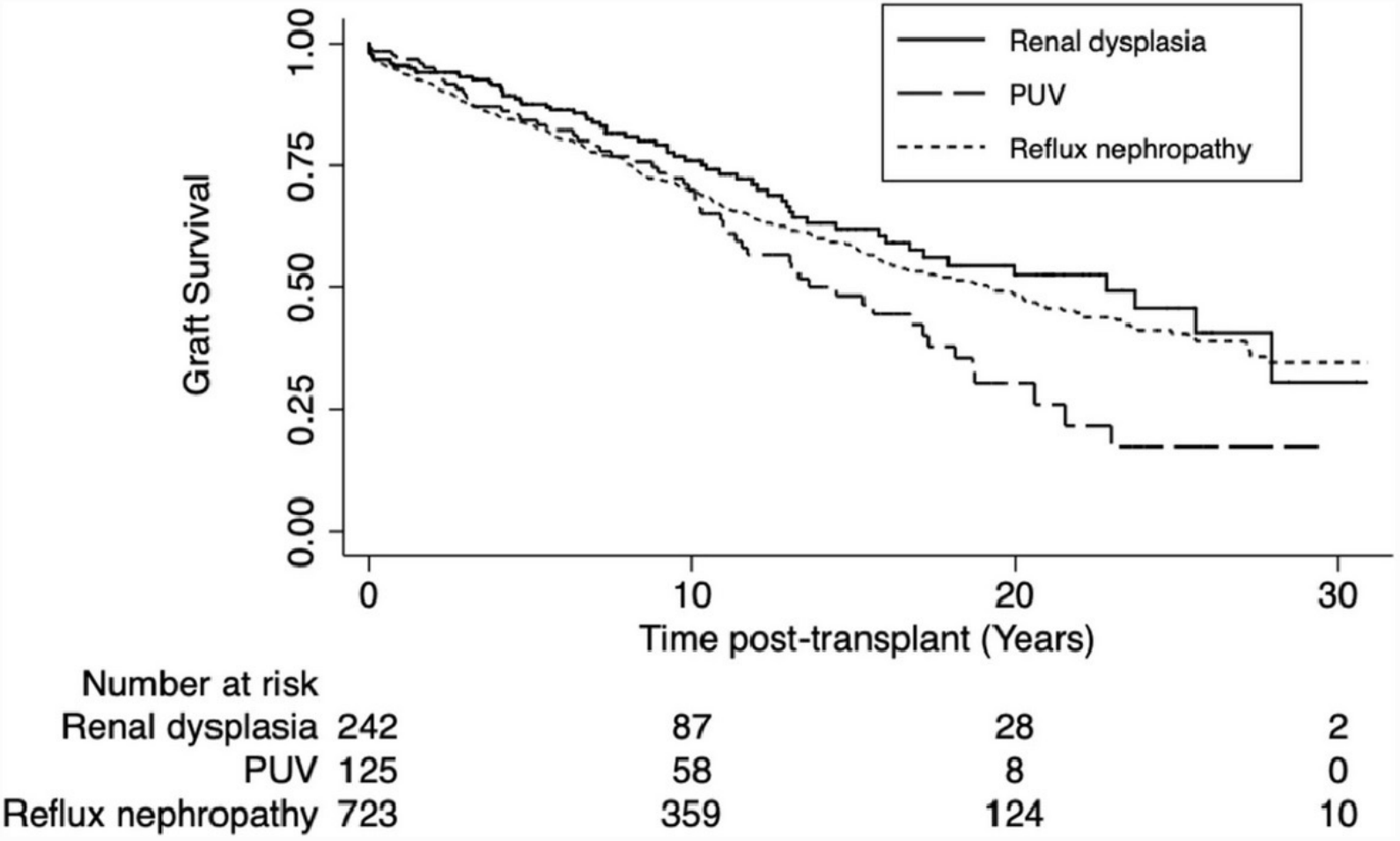


FIGURE 2 | Long-term graft survival (Kaplan–Meier analysis) in patients who did and did not undergo the Mitrofanoff procedure.

Fig. 1

From: Long-term outcome of kidney transplantation in patients with congenital anomalies of the kidney and urinary tract



Kaplan-Meier analysis of a death-censored graft survival stratified by primary renal disease

McKay, A.M., Kim, S. & Kennedy, S.E. Long-term outcome of kidney transplantation in patients with congenital anomalies of the kidney and urinary tract. *Pediatr Nephrol* **34,** 2409–2415 (2019).

Summary

- Antenatal diagnosis and treatment of PUV is possible, but recent data failed to show long time benefits for future renal function
- PUV diagnosis carries a 50% long-term risk of CKD and 20-30% of ESRD by the age of 18 years
- Bladder dysfunction are common in patients with PUV and in most cases evolve with time from small low compliant bladder to the large distended bladder unable to empty
- Careful bladder evaluation before kidney Tx and introduction of CIC or augmentation cystoplasty may improve graft survival

NEXT WEBINARS

25/01/22

Renal tubular dysgenesis,
Laurence Heidet (Paris, France)

01/02/22

KDIGO Guideline on Immune GP I,
Jack Wetzels (Nijmegen, Netherlands)

08/02/22

Focal segmental glomerulosclerosis
Emmanuelle Plaisier (Paris, France)

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