WEBINAR

21/02/23

Welcome to

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

Dysplasia guideline & LUTO guideline

Speaker: Stefan Kohl (Cologne, Germany) and
Valentina Capone (Milan, Italy)

Moderator: Francesco Emma (Rome, Italy)

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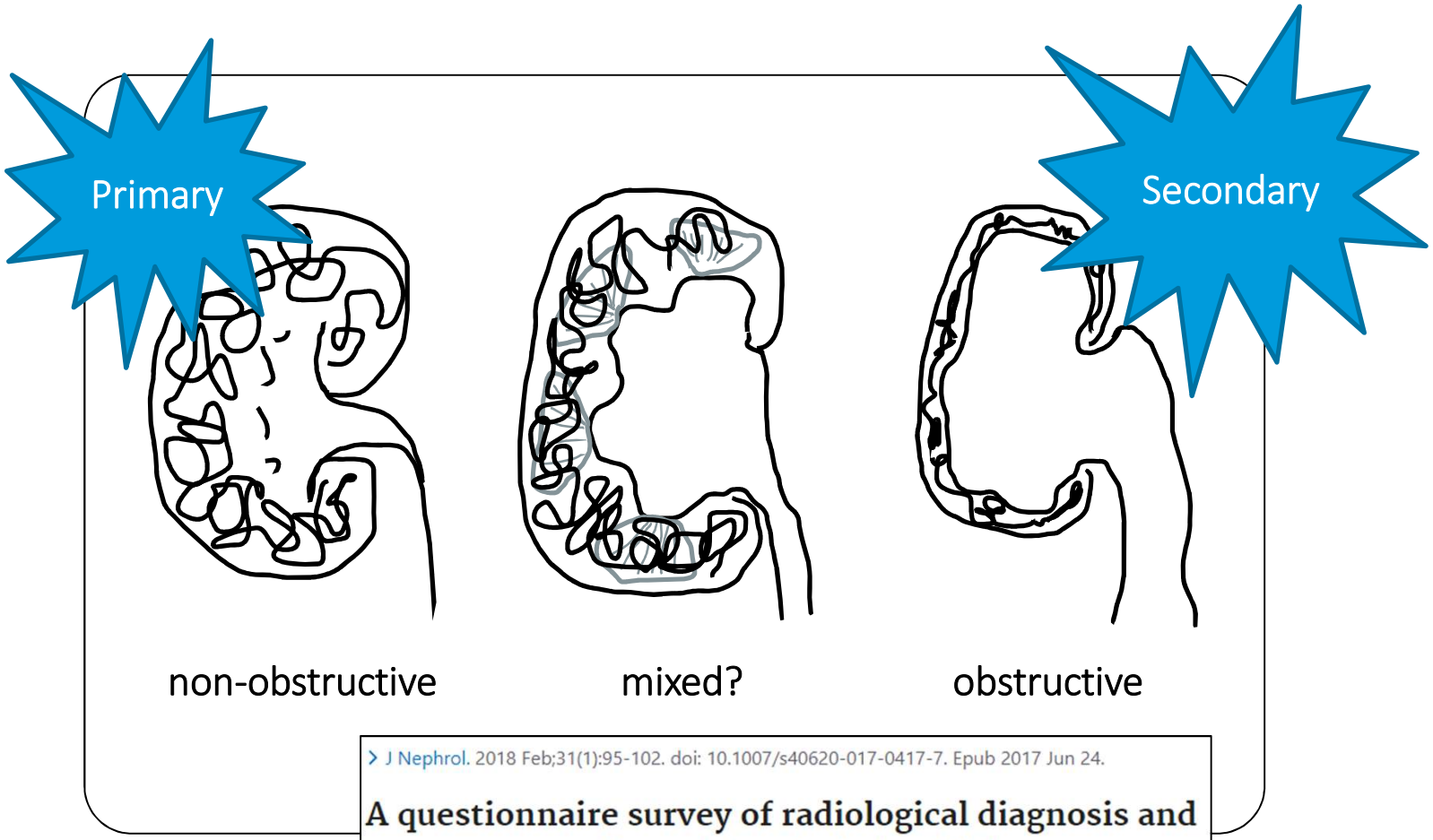
Non-obstructive kidney dysplasia- Clinical diagnosis and management

ERKNet Postgraduate Curriculum in Rare Kidney Diseases

ESPN – IPNA Curriculum in Pediatric Nephrology

PD Dr. Stefan Kohl, ESPN fellow, University of Cologne

Kidney dysplasia- same, same, but different?



> J Nephrol. 2018 Feb;31(1):95-102. doi: 10.1007/s40620-017-0417-7. Epub 2017 Jun 24.

A questionnaire survey of radiological diagnosis and management of renal dysplasia in children

Giovanni Montini [1], Marco Busutti [2], Fatos Yalcinkaya [3], Adrian S Woolf [4], Stefanie Weber [5]; European Society for Paediatric Nephrology Working Group on Congenital Anomalies of the Kidney and Urinary Tract

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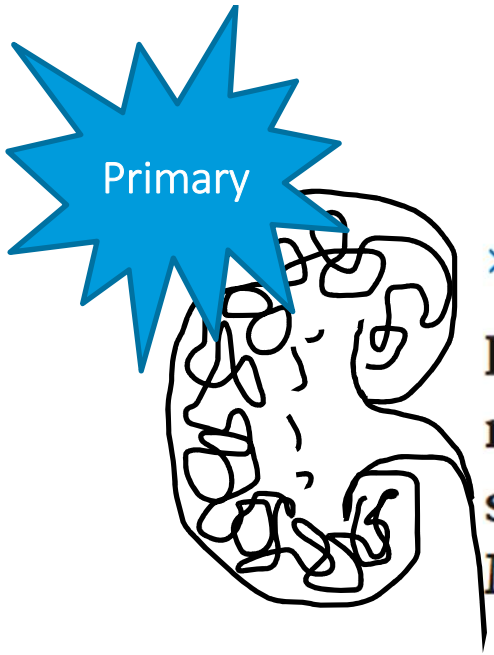

> Nephrol Dial Transplant. 2022 Nov 23;37(12):2351-2362. doi: 10.1093/ndt/gfac207.

Definition, diagnosis and clinical management of non-obstructive kidney dysplasia: a consensus statement by the ERKNet Working Group on Kidney Malformations

Stefan Kohl [1], Fred E Avni [2], Peter Boor [3 4], Valentina Capone [5], William L Clapp [6], Diego De Palma [7], Tess Harris [8], Laurence Heidet [9 10], Alina C Hilger [11 12], Helen Liapis [13], Marc Lilien [14], Gianantonio Manzoni [15], Giovanni Montini [5 16], Susanna Negrisolo [17], Marie-Jeanne Pierrat [18], Ann Raes [19], Heiko Reutter [12 20], Michiel F Schreuder [21], Stefanie Weber [22], Paul J D Winyard [23], Adrian S Woolf [24 25], Franz Schaefer [26], Max C Liebau [1 27 28 29]

Affiliations + expand

PMID: 35772019 PMCID: PMC9681917 DOI: 10.1093/ndt/gfac207

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Poll question: How many patients with bilateral kidney dysplasia do you currently treat?

a) None
b) <10
c) 10-20
d) >20

CAKUT/dysplasia account for 50% of pediatric CKD

Table 1 Selected studies on the causes of chronic kidney disease in children

	Causes of CKD			Causes of ESRD			
Study [reference]	NAPRTCS [12]	Italian Registry [5]	Belgian Registry [13]	ANZDATA [27]	ESPN/ERA-EDTA Registry [28]	UK Renal Registry [29]	Japanese Registry [30]
Population	CKD (GFR<75)	CKD (GFR<75)	CKD (GFR<60)	ESRD (RRT)	ESRD (RRT)	ESRD (RRT)	ESRD (RRT)
Age range	0–20	0–19	0–19	0–19	0–15	0–15	0–19
Patients	Registered 1994–2007	Incident 1990–2000	Incident 2001–2005	Incident 2003–2008	Incident 2008	Incident 2004–2008	Prevalent 1998
Number of cases	7,037	1,197	143	369	499	428	582
Etiology							
CAKUT	3,361 (48%)	689 (58%)	84 (59%)	127 (34%)	182 (36%)	184 (43%)	208 (36%)
Hypodysplasia±reflux nephropathy	1,907	516	66	95		135	198
Obstructive uropathy	1,454	173	18	32		49	10
Glomerulonephritis	993 (14%)	55 (5%)	10 (7%)	108 (29%)	76 (15%)	78 (18%)	130 (22%)
HUS	141 (2%)	43 (4%)	9 (6%)	9 (2%)	29 (6%)		13 (2%)
Hereditary nephropathy	717 (10%)	186 (15%)	27 (19%)		112 (22%)		69 (12%)
Congenital NS	75	13	5	7		15	34
Metabolic disease			5		17	18	
Cystinosis	104	22	2	4			2
Cystic kidney disease	368 (5%)	101 (8%)	13 (9%)	25 (7%)	59 (12%)	49 (11%)	35 (6%)
Ischemic renal failure	158 (2%)	49 (4%)	3 (2%)	8 (2%)	11 (2%)		11 (2%)
Miscellaneous	1,485 (21%)	122 (10%)	10 (7%)	65 (18%)	52 (10%)	19 (4%)	83 (14%)
Missing/unknown	182 (3%)	40 (3%)		16 (4%)	37 (7%)	65 (15%)	34 (6%)

CKD, chronic kidney disease; ESRD, end-stage renal disease; RRT, renal replacement therapy; GFR, glomerular filtration rate (ml/min/1.73 m^2); CAKUT, congenital anomalies of the kidney and urinary tract; NS, nephrotic syndrome; HUS, hemolytic uremic syndrome; NAPRTCS, North American Pediatric Renal Trials and Collaborative Studies; ANZDATA, Australia and New Zealand Dialysis and Transplant Registry; ESPN/ERA-EDTA Registry, European Registry for Children on Renal Replacement Therapy

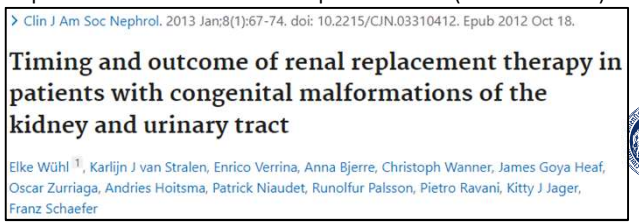
Harambat et al, *Pediatr Nephrol* (2012)

Severely dysplastic kidneys fail early

	Age at transplantation				
	0-1 y (%)	2-5 y (%)	6-12 y (%)	13-17 y (%)	≥18 y (%)
Gender					
Male	70.0	65.2	58.0	56.0	54.3
Female	30.0	34.8	42.0	44.0	45.7
Primary diagnosis					
Renal plasias	27.5	23.3	16.4	11.4	9.8
Obstructive uropathy	19.6	20.2	15.6	13.2	9.9
Other	52.4	48.7	55.6	62.3	63.9
FSGS	0.6	7.7	12.4	13.1	16.4

CAKUT/dysplasia

adopted from NAPRTCS report 2018 (Chua et al.)



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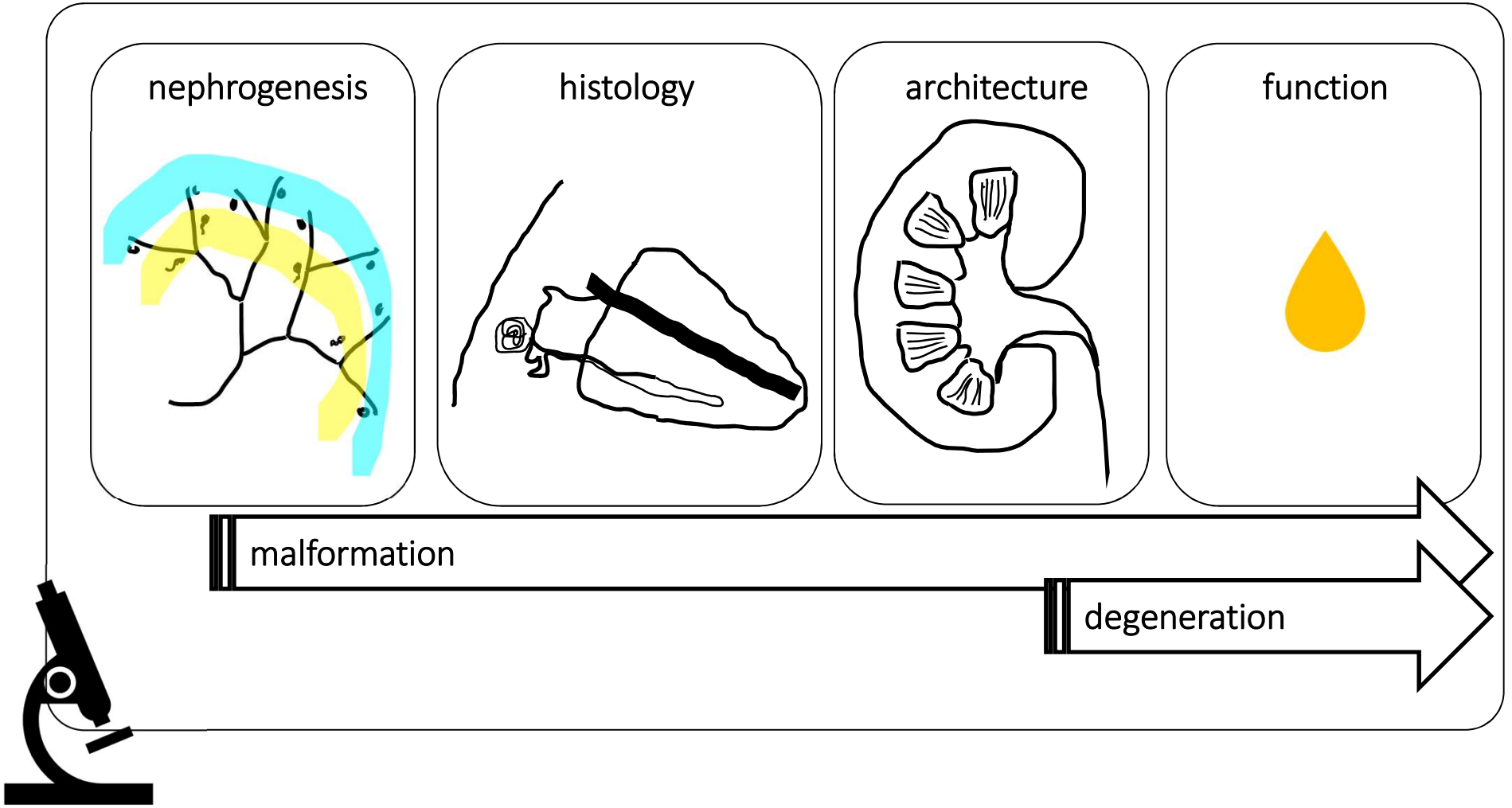
Dysplasia- the absence of “normal“…



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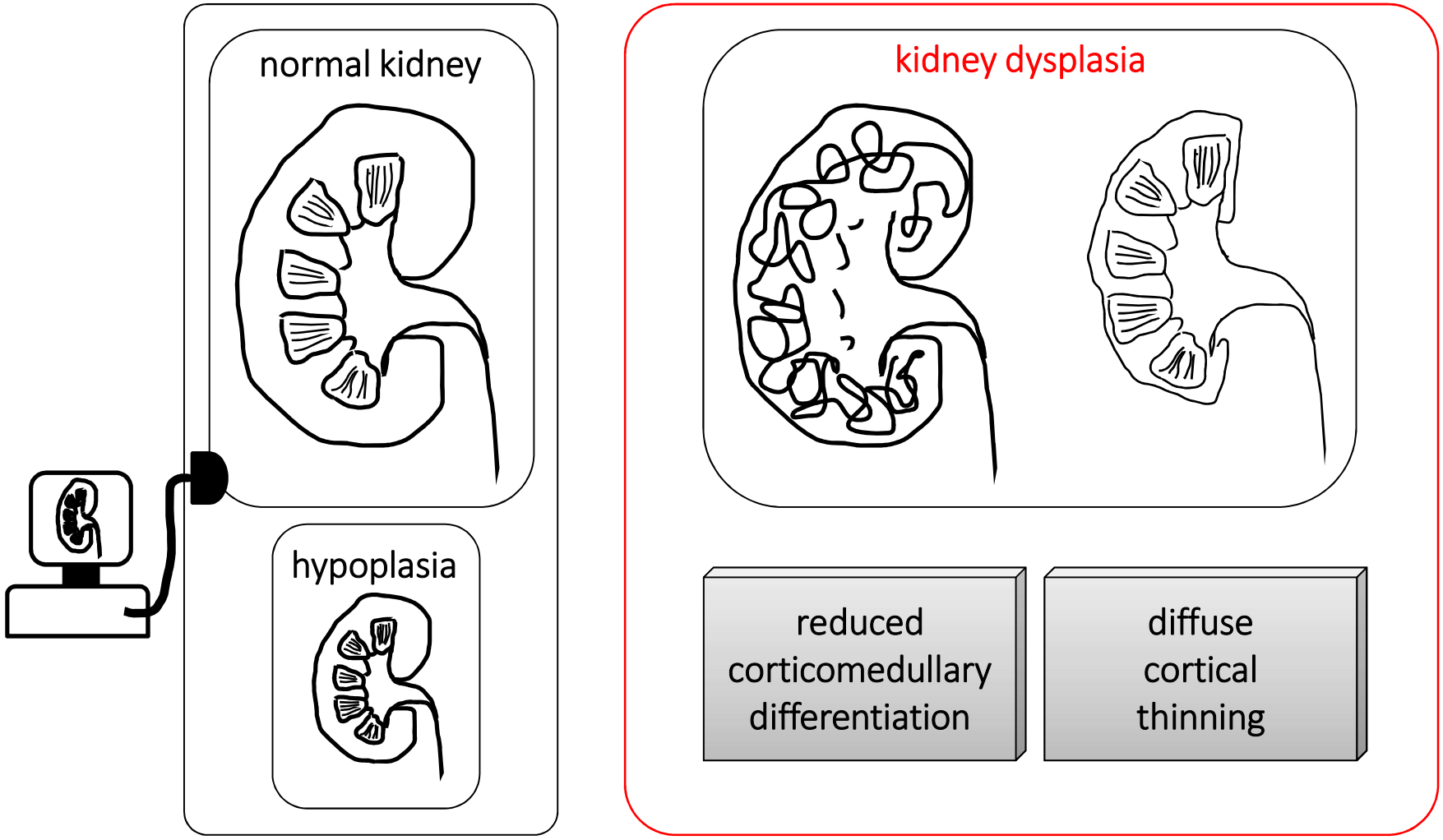
The clinical diagnosis of kidney dysplasia



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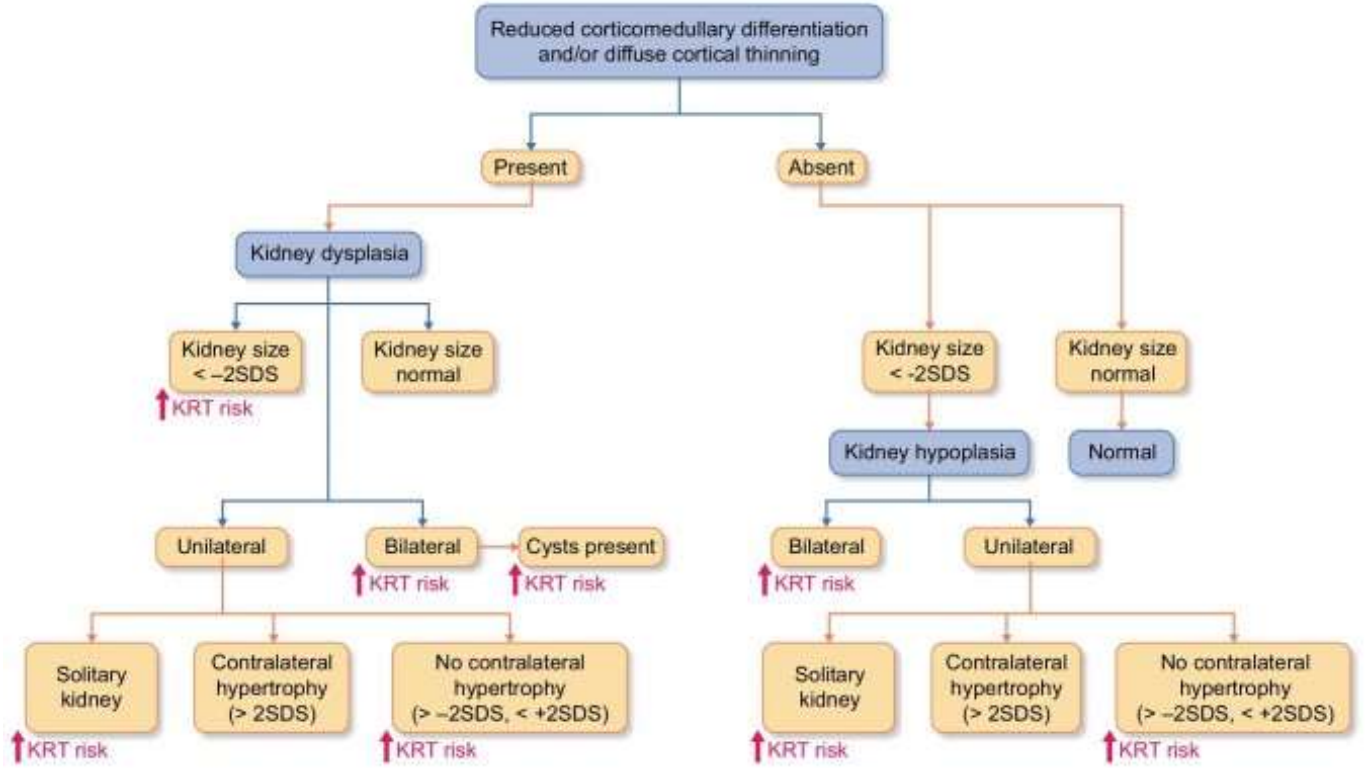
Kidney dysplasia: Sonographic risk assessment



Kohl et al., *Nephrol Dial Transplant.*, 2022

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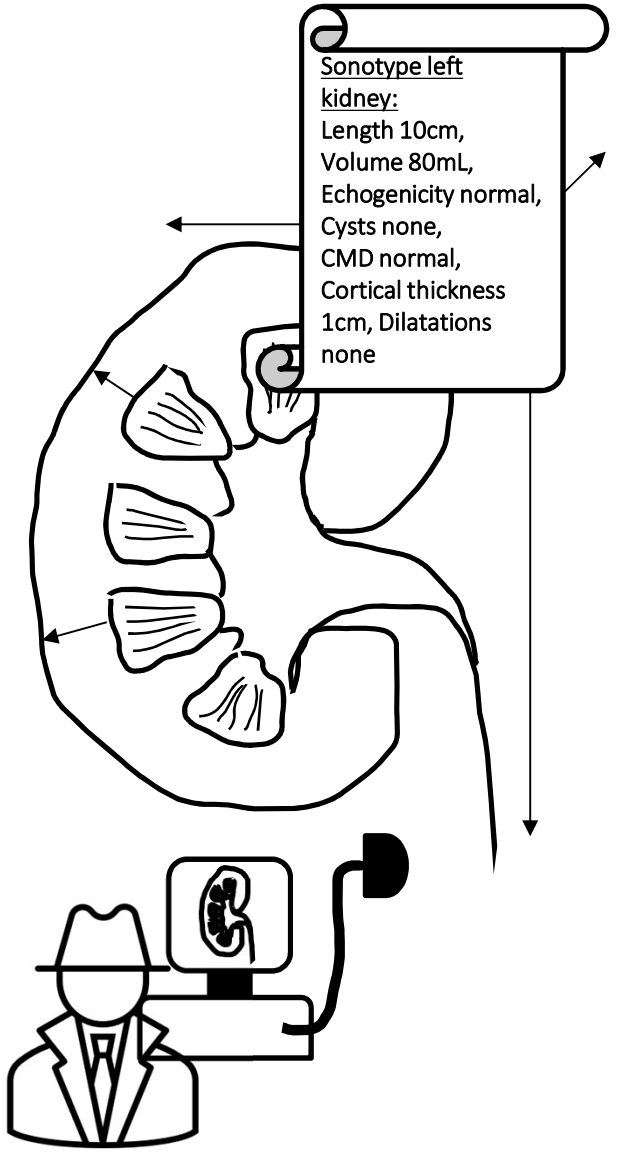
The kidney “sonotype"

- Area (*Prenatal*: Amniotic Fluid)
  - length, volume
- Brightness
  - echogenicity normal, increased
- Cysts & Circulation
  - None, single, few, multiple
  - localization of cysts?
  - If possible: Vascular patency (Doppler)
- Differentiation, corticomedullary
  - normal, reduced, absent
- Edge
  - cortical thickness, diffuse cortical thinning
- Flow
  - diameter of renal pelvis (transversal plane)
  - *Prenatal*: Bladder volume



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Kidney dysplasia: clinical management

Diagnostic workup

- Bilateral disease? eGFR baseline?
- Involvement of other organs?
- VCUG not routinely required
- Scintigraphy not routinely required
- Genetic testing in selected cases

Therapy: Prevent progression of CKD

- Treat microalbuminuria (RAAS inhibitors)
- Treat hypertension
- Treat other complications of CKD
- Avoid urinary tract infections and additional kidney injuries

- Kidney replacement therapy

Genetic testing in monogenic CAKUT/dysplasia

- Less than 5% of all CAKUT are monogenic
- In selected cohorts 20%+ of CAKUT are monogenic
- Consider genetic testing in
  - severe CAKUT
  - familial CAKUT
  - syndromic CAKUT
- Diagnostic genetic testing in LUTO not recommended
- We suggest testing by WES with in-silico filtered ”kidney panel” and CNV analysis
- Kidney dysplasia/hypoplasia cannot be differentiated genetically
- Genetic testing and counseling in CAKUT is challenging (variable expressivity, incomplete penetrance, questionable “CAKUT genes”)

Nicolaou et al, *KI* 2015
Hwang et al, *KI* 2014
Ahn et al, *J Clin Med* 2020
Heidet et al, *JASN* 2017

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Kidney dysplasia: Prenatal counseling

- Postnatal course and kidney function cannot be predicted accurately
- Think and speak in terms of “more likely or less likely”
- Re-evaluate throughout pregnancy as situation may change
- Amniotic fluid volume and lung size as predictor for lung hypoplasia
- We do not recommend prenatal testing for variants in “CAKUT genes”
- In syndromic CAKUT, consider prenatal genetic testing for chromosomal aberrations

© Kohl & Liebau, *Kidney360*, editorial, accepted

Thank you!

Kidney dysplasia: prognosis

EXHIBIT 14.2
CKD TERMINATION BY SELECTED PATIENT CHARACTERISTICS AT BASELINE (continued)

	Number of Patients	Number of Terminations	Percent Terminations	Reason for Termination (%)				
				Transplant	Dialysis	Native Function Returned	Death	Other/ Unknown
Primary Diagnosis								
Obstructive Uropathy	1454	648	44.6	40.4	45.4	3.5	2.0	8.6
Renal Plasias	1220	576	47.2	42.5	45.3	3.0	4.2	5.0
Reflux Nephropathy	594	196	33.0	39.3	43.9	3.1	1.5	12.2
FSGS	613	368	60.0	19.0	73.1	1.6	1.1	5.2
Other/Unk/Missing	3156	1448	45.9	31.7	53.0	3.0	5.1	7.2

NAPRTCS 2008

5 years follow up: Almost 50% of patients on KRT

Kidney dysplasia is the most frequent cause for CKD in children

NAPRTCS 2008
Chronic Kidney Disease

EXHIBIT 13.1B
CKD PRIMARY DIAGNOSIS

	All Patients		Renal Biopsy Confirmed Diagnosis	
	N	%	N	%
Total	7037	100.0	6631	29.8
Primary Diagnosis				
Obstructive uropathy	1454	20.7	1399	8.1
A/hypo/dysplastic kidney	1220	17.3	1154	7.0
FSGS	613	8.7	604	93.9
Reflux nephropathy	594	8.4	566	7.1
Polycystic disease	278	4.0	265	20.0

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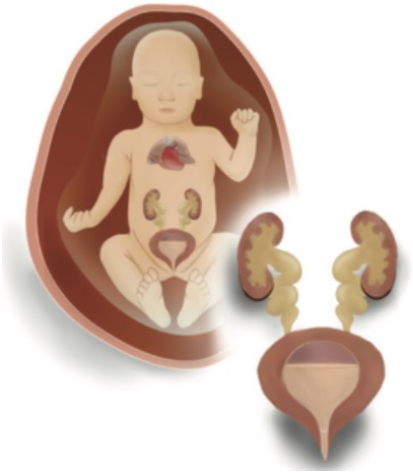
ERKNeT Consensus Statement on fetal LUTO

Valentina Capone

Pediatric Nephrology, Dialysis and Transplant Unit
Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico
Milano

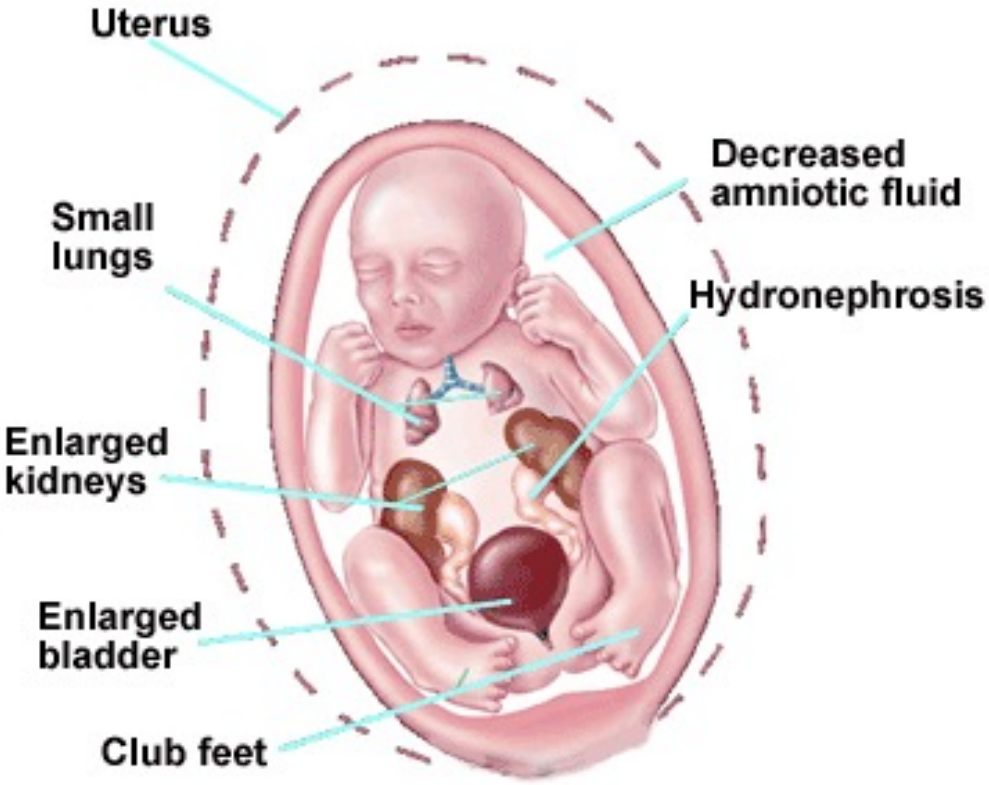
Fetal lower urinary tract obstruction (LUTO)

Obstruction to flow of urine from fetal bladder



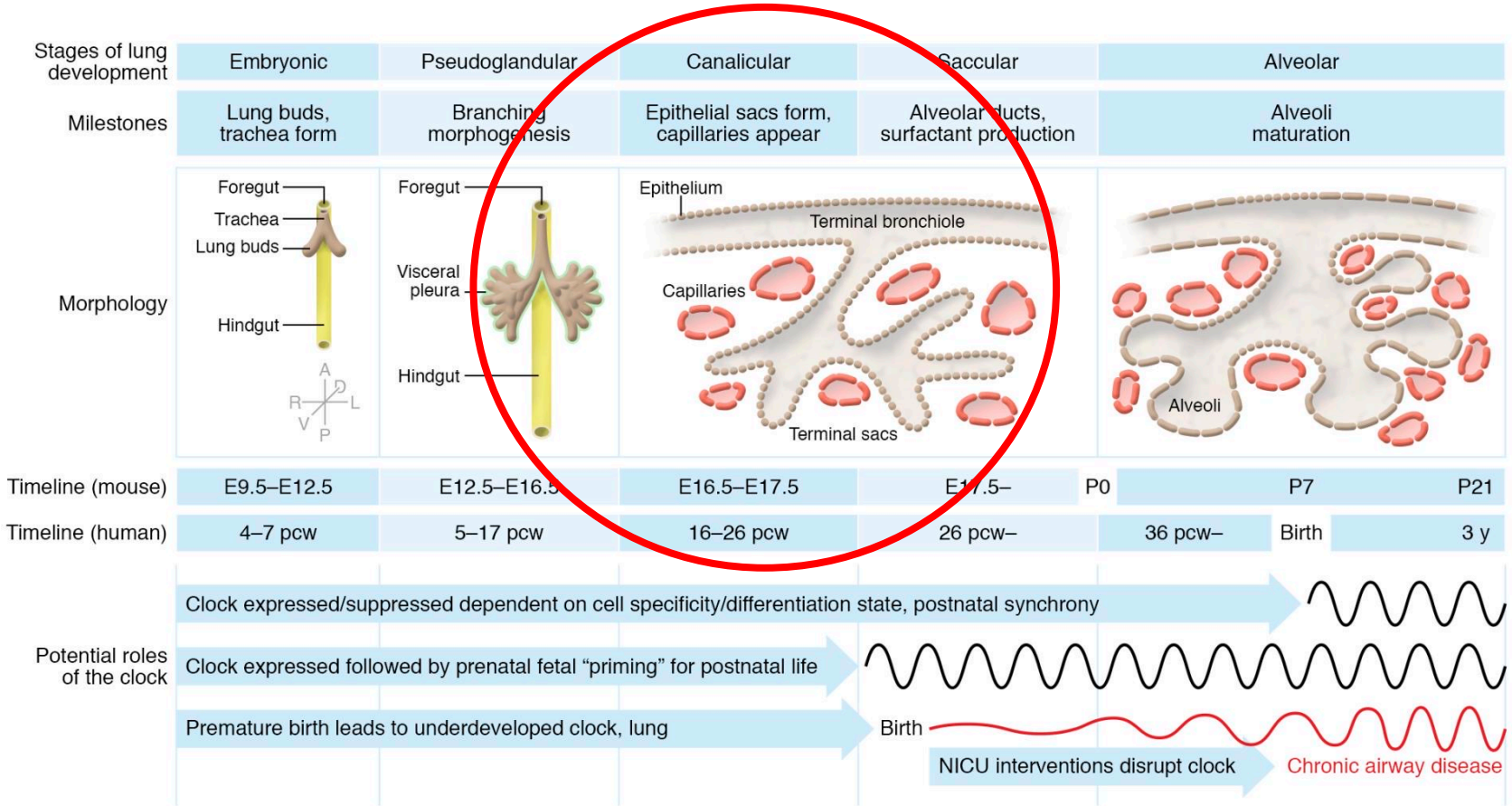
- 2-3/10,000 fetuses
- 1:1 prenatal:postnatal diagnosis
- Causes: ++ posterior urethral valves, urethral atresia
- Other causes: anterior urethral valves, megalourethra, cloacal malformations and prolapsing ureterocele

Consequences of fetal LUTO



- progressive bladder dilation and bladder wall thickening
- subsequent hydro-ureteronephrosis
- kidney parenchymal compression
- Oligohydramnios/anhydramnios

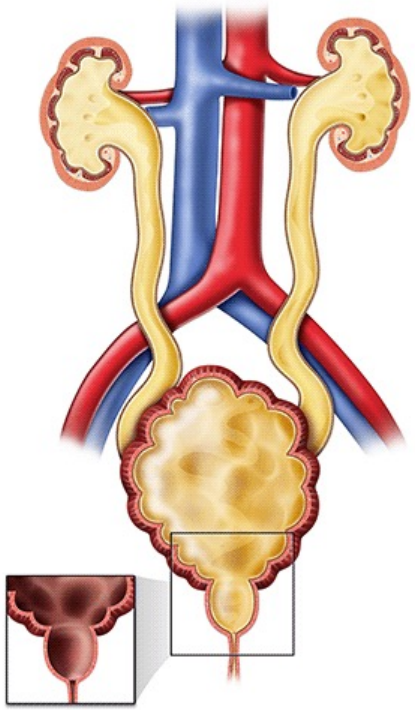
Lung hypoplasia



60-80% mortality if diagnosed in the second trimester of gestation
Lifetime risk of developing ESKD ~30%

Kidney damage

- Direct compression of kidney parenchima
- Gene mutations



Lack of guidelines on fetal LUTO

- Diagnostic features
- Differential diagnosis
- Prediction of postnatal outcome
- Benefits and limits of fetal intervention

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European Reference Networks

Co-funded by the European Union

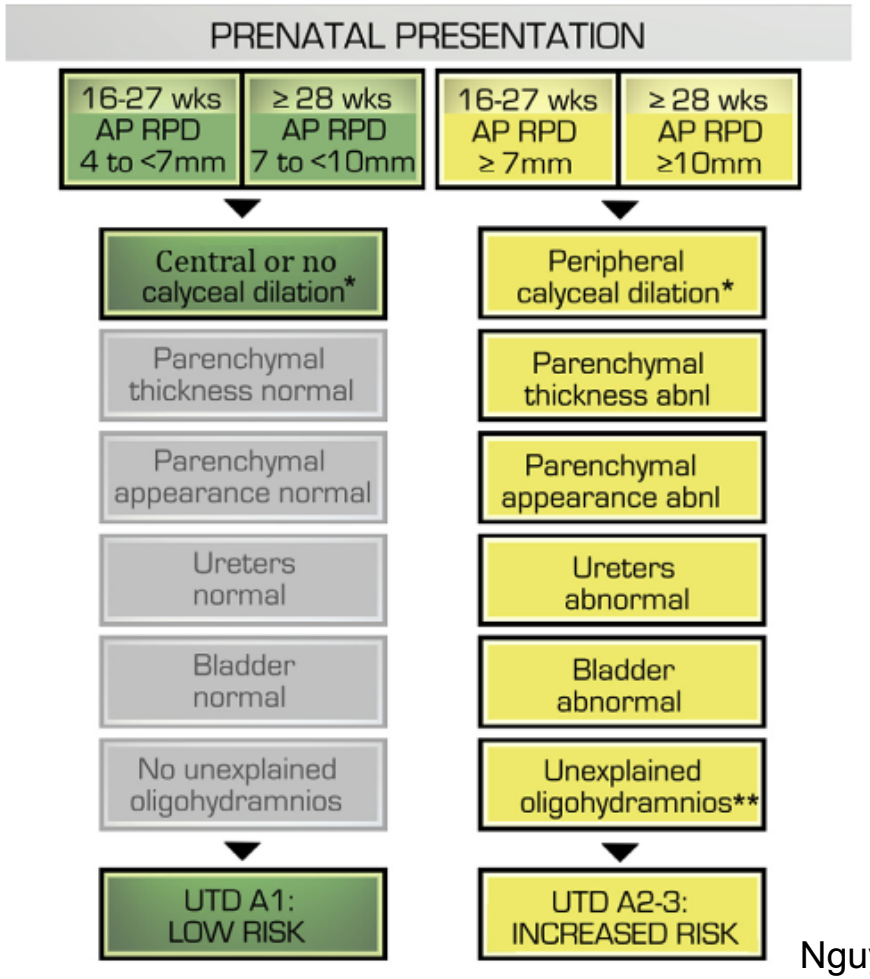
CONSENSUS STATEMENT

Check for updates

Definition, diagnosis and management of fetal lower urinary tract obstruction: consensus of the ERKNet CAKUT-Obstructive Uropathy Work Group

Nature Reviews Urology 2022

Prenatal diagnosis: APD



UTD classification
Nguyen et al, Pediatric Urology 2014

Prenatal diagnosis – poll question

What prenatal ultrasonographic feature is more suggestive of lower urinary tract obstruction?

- Bilateral hydronephrosis
- Anhydramnios
- Enlarged bladder
- Kidney cysts

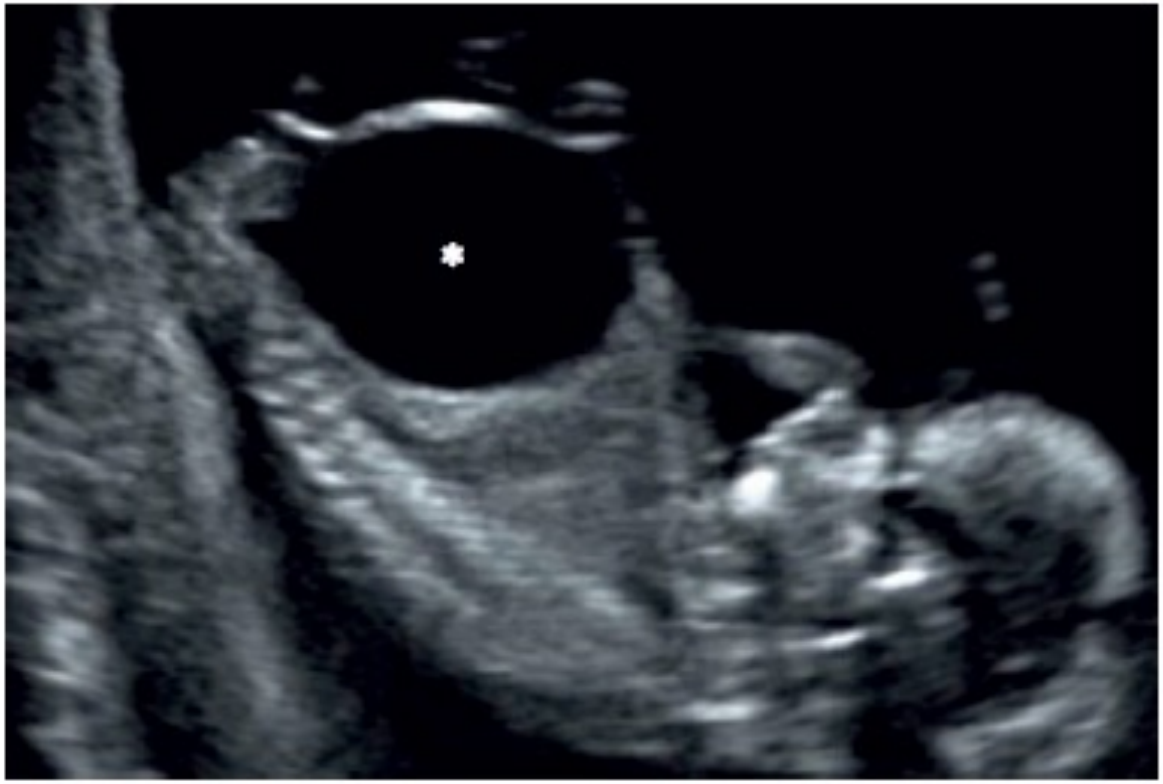
Prenatal diagnosis: megacystis

I trimester:

- longitudinal bladder diameter ≥7 mm
- 7-12 mm resolves in ~ 90% of cases
- ≥15 mm strongly suggestive of LUTO

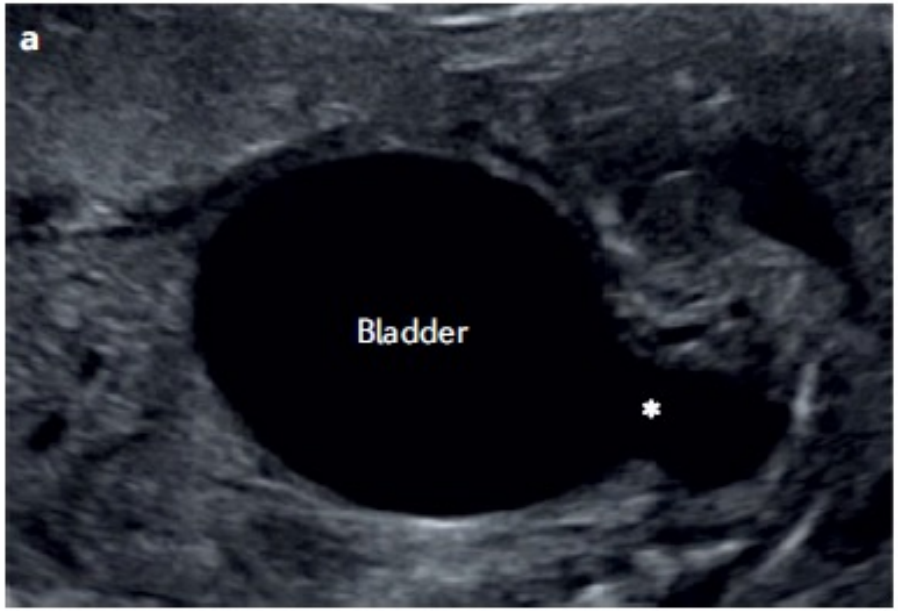
II trimester:

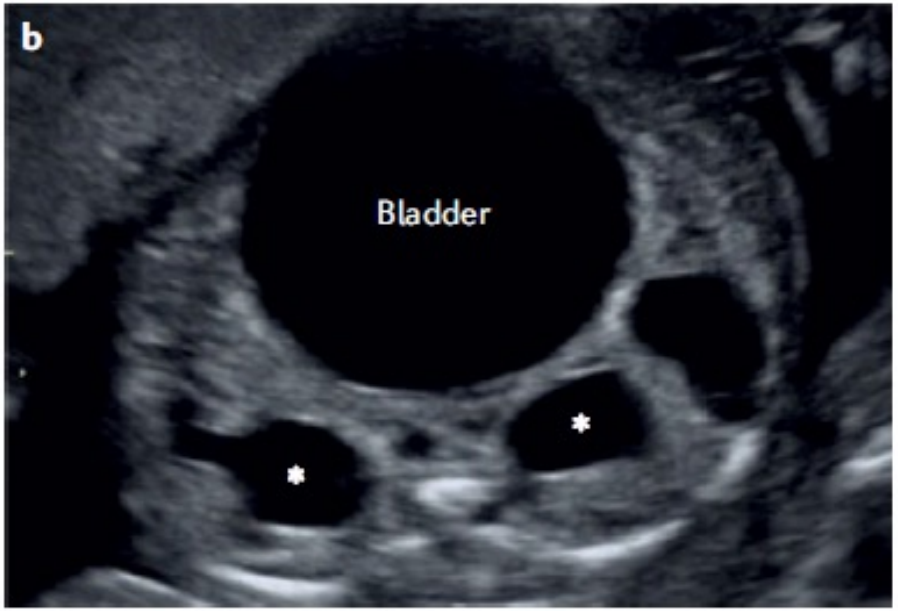
- bladder that fails to void over 40 mins



Prenatal diagnosis

Classical triad: megacystis, keyhole sign and bilateral hydronephrosis





Prenatal diagnosis

143 fetuses with megacystis
18 weeks' gestation onwards

Variable	*Points*
Severe megacystis*	4
Bilateral ureteral diameters	1.3/mm†
Oligo- or anhydramnios	4
Male fetal sex	4
Referral < 28 weeks	4

Score of ≥ 9.5 indicates LUTO. *Bladder volume > 35 cm^3 or ascites. †Value for each mm of ureteral size.

> than classical triad in identifying LUTO vs non obstructive megacystis

Fontanella et al, Ultrasound Obstet Gynecol, 2018

Prenatal diagnosis

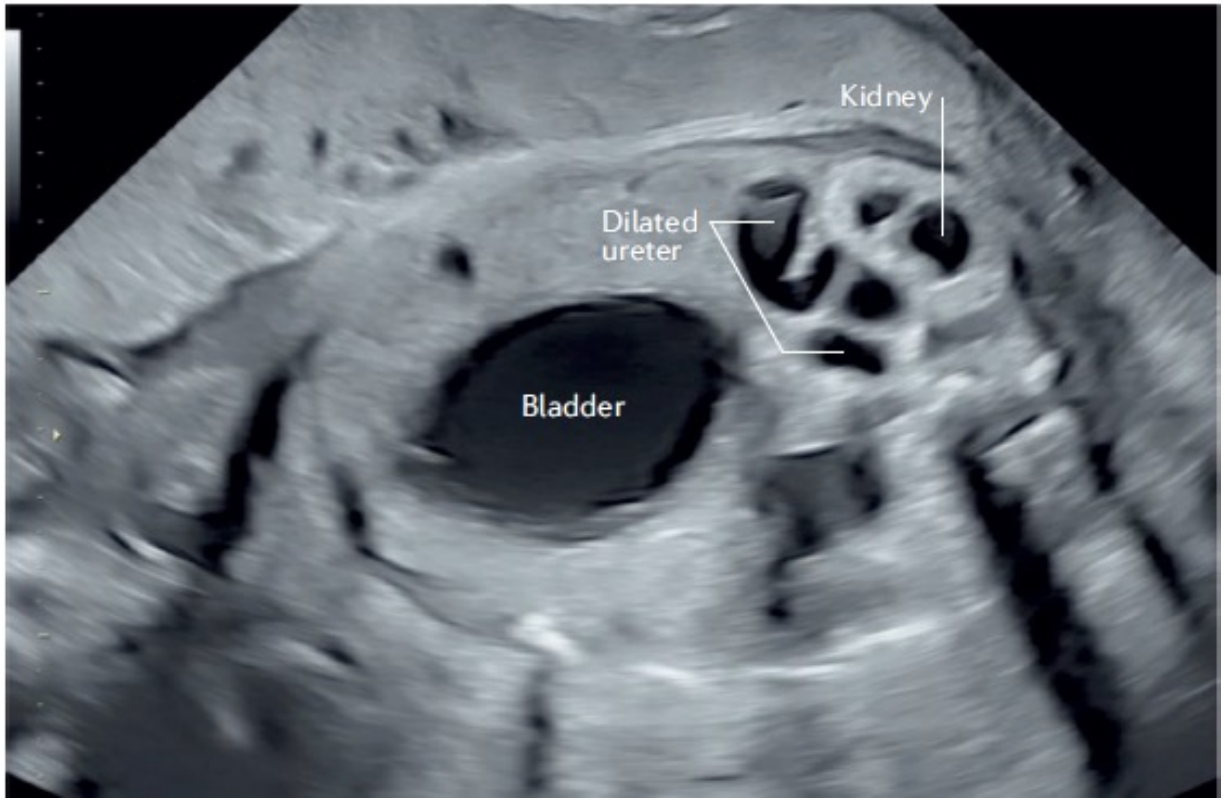
Recommendation 1

The most reliable parameter for suspecting the presence of obstructive uropathy is the antero-posterior diameter (APD) of the renal pelvis, as proposed by the Urinary Tract Dilation (UTD) classification. Pelvic dilation is defined by an APD ≥7 mm at 16–27 weeks and ≥10 mm at ≥28 weeks' gestation. An APD of 4–6 mm at 16–27 weeks and 7–9 mm at ≥28 weeks' gestation should be given clinical consideration prenatally only if associated with other signs of obstructive uropathy.

Recommendation 2

Prenatal suspicion of lower urinary tract obstruction (LUTO) requires the presence of an enlarged fetal bladder (megacystis) on obstetric ultrasound scan at any stage during pregnancy. In the first trimester, fetal megacystis (defined as a longitudinal bladder diameter of ≥7 mm) is strongly suggestive of LUTO if the longitudinal bladder diameter is ≥15 mm. Further research is needed to objectively define bladder enlargement during the second and third trimesters and to differentiate between obstructive and non-obstructive causes of prenatal megacystis through the development of a reliable severity scoring system.

Outcome prediction: survival



Outcome prediction: survival

Table 4—Prognostic variables for survival of live born children

Postnatal course	Alive $N = 10$	Neonatal death $N = 15$	P value
Maternal age >36 years	2	2	1.00
GA delivery (weeks: median, range)	35.3 (34.3–38.5)	34.6 (31–39.5)	0.24
GA oligohydramnios	32.2 (25.2–37.3)	28.1 (18.3–35.5)	0.02
Birth weight (g)	2617 (1830–3730)	2535 (1700–3300)	0.77
Renal diagnosis	1	5	0.05[a]
Dysplasia	2	6	0.08
Polycystic	7	4	0.04
Hydronephrosis	1	7	0.05
Anhydramnios	9/1	7/8	0.67
Isolated renal anomaly/+other structural or chromosomal abnormalities	0	5	0.002
Diagnosis <24 weeks	0	10	0.04
Apgar score 5 min ≤5	1	8	
Ventilatory support	4	2	1.00
No/not started	5	5	0.46
CPAP, SIMV, or conventional pressure ventilation	3/9	3/7	
HFO or ECMO	5 (1–17)	1 (0–14)	
Pneumothorax (/ventilatory support)			
Duration ventilatory support (days, median(range))			

Grijseels E.W.M., Prenatal Diagnosis 2011

Kidney function prediction – poll question

What is the most reliable predictor of postnatal kidney function?

- Anhydramnios before 20 weeks of gestation
- Fetal blood beta2microglobulin
- Fetal urine beta2microglobulin
- Kidney dysplasia

Outcome prediction: kidney function

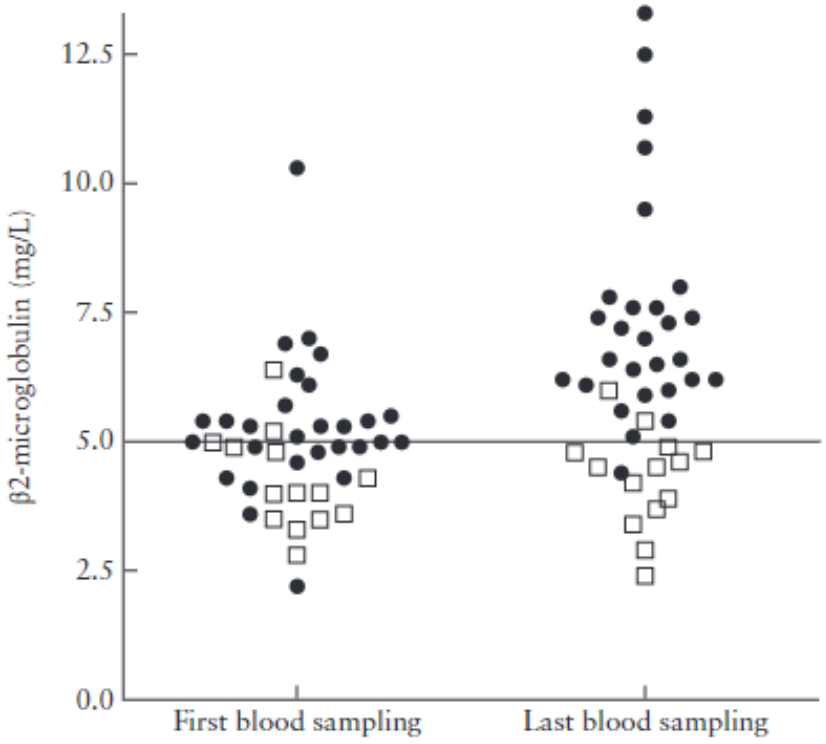
Table 3. Subgroup meta-analysis (random effects model) of antenatal ultrasound diagnostic measures to predict poor postnatal renal function in survivors with congenital lower urinary tract obstruction

Diagnostic measure	Sensitivity (95% confidence intervals)	Specificity (95% confidence intervals)	Chi-square test (*P* value)	Area under receiver operating characteristic curve
Oligohydramnios	0.63 (0.51–0.74)	0.76 (0.65–0.85)	19.67, (0.02)	0.74
Renal cortical appearance	0.57 (0.37–0.76)	0.84 (0.71–0.94)	10.29, (0.04)	0.78
Gestation at diagnosis <24 weeks	0.48 (0.26–0.70)	0.82 (0.66–0.92)	3.88, (0.14)	0.68

Morris RK, BJOG 2009

Outcome prediction: kidney function

42 fetuses with LUTO



Measurement	*Sensitivity*	*Specificity*
β2m		
First sampling	18/28 (64.3)	11/14 (78.6)
Last sampling	27/28 (96.4)	12/14 (85.7)
AFV		
First sampling	10/28 (35.7)	10/14 (71.4)
Last sampling	21/28 (75.0)	9/14 (64.3)

Data are given as *n*/*N* (%).

Spiaggiari E, Ultrasound Obstet Gynecol 2017

Kidney function prediction – poll question

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- Fetal blood beta2microglobulin
- Fetal urine beta2microglobulin
- Kidney dysplasia
- **NONE OF THE ABOVE**

Outcome prediction

Recommendation 3
The risk of fetal and neonatal death has to be based on the presence of oligohydramnios or anhydramnios before 20 weeks' gestation, which is a strong predictor of pulmonary hypoplasia.

Recommendation 4
The risk of kidney replacement therapy cannot be foreseen before birth, as amniotic fluid volume, kidney parenchymal echogenicity and fetal urine biomarkers are not reliable predictors. Normal postnatal kidney function is also not predictable by a normal amount of amniotic fluid.

Staging of severity - 1

	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

SURVIVAL:	100%	75% with VAS	14% no VAS
ESKD 6 months:	0%	33%	100%

Ruano R, Ultrasound Obstet Gynecol 2016

Staging of severity - 1

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SURVIVAL:	100%	75% with VAS	14% no VAS
ESKD 6 months:	0%	33%	100%

Ruano R, Ultrasound Obstet Gynecol 2016

Staging of severity - 2

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

Fontanella F, Ultrasound Obstet Gynecol 2019

Staging of severity - 2

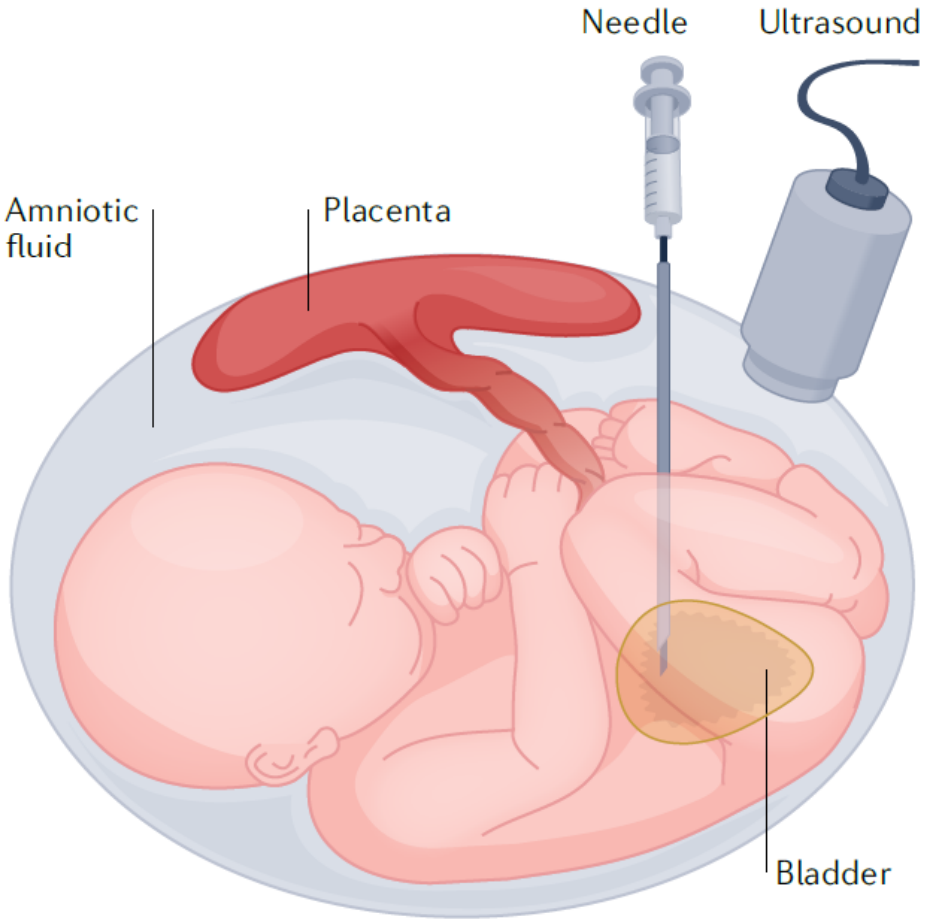
Variable	LUTO stage		
	Severe (n = 33)	*Moderate* (n = 38)	*Mild* (n = 70)
Perinatal mortality	18 (54.5)	10 (26.3)	6 (8.6)
GA at appearance of oligo- or anhydramnios (weeks)	21 ± 8	29 ± 8	35 ± 4
ARCA	26 (78.8)	26 (68.4)	24 (34.3)
Mean eGFR (mL/min/1.73 m^2)†	65 ± 47	57 ± 44	87 ± 43
Severely impaired renal function†‡	4/9 (44.4)	5/16 (31.3)	4/36 (11.1)

Fontanella F, Ultrasound Obstet Gynecol 2019

Staging of severity

Recommendation 5
Multi-parameter scoring systems to stage the severity of LUTO and to predict postnatal outcome have been proposed, but have not yet been clinically adopted. Further clinical validation and the adoption of standardized assessment across prenatal centres are needed.

Fetal surgical management: VAS



COMPLICATIONS: 40%

- shunt dislocation or retraction
- shunt blockage
- fetal ascites
- premature rupture of membranes
- preterm labour
- abdominal wall herniation
- fetal demise

Capone, Nature Reviews Urology 2022

Fetal surgical management: VAS

Ultrasound Obstet Gynecol 2017; 49: 696–703
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.15988

Effectiveness of vesicoamniotic shunt in fetuses with congenital lower urinary tract obstruction: an updated systematic review and meta-analysis

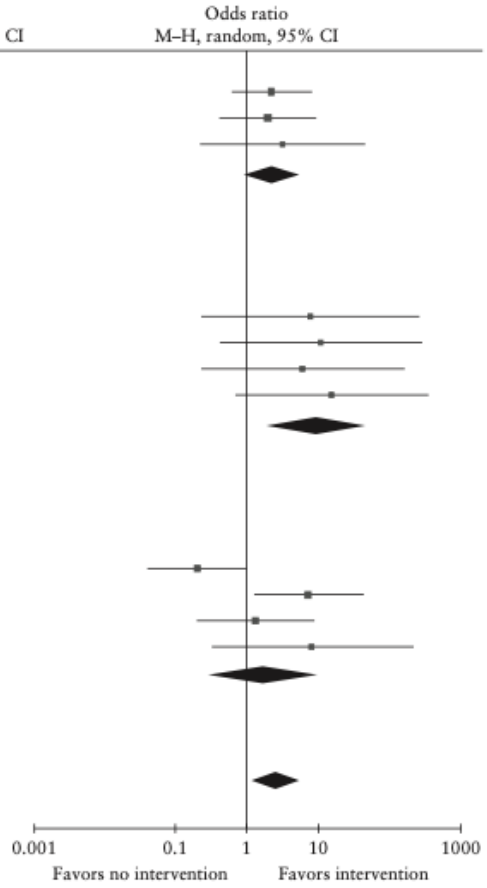
A. A. NASSR[1,2,3#], S. A. M. SHAZLY[1,2#], A. M. ABDELMAGIED[1,2], E. ARAUJO JÚNIOR[4], G. TONNI[5], M. D. KILBY[6] and R. RUANO[7]

- 9 studies
- 246 fetuses
- VAS 20-27 wks vs conservative management
- Up to 2 yrs follow up

Fetal surgical management: VAS

Perinatal survival (6 months)

Study or subgroup	Intervention Events	Intervention Total	No intervention Events	No intervention Total	Weight (%)	Odds ratio M–H, random, 95% CI
Cases selected by 'favorable' fetal urinary biochemistry						
Ruano (2015)[9]	7	13	12	35	16.7	2.24 (0.61–8.16)
Freedman (1996)[25]	14	21	5	10	14.2	2.00 (0.43–9.29)
Crombleholme (1990)[21]	8	9	5	7	7.0	3.20 (0.23–45.19)
Subtotal (95% CI)		43		52	37.8	2.24 (0.89–5.67)
Total events	29		22			
Heterogeneity: $tau^2 = 0.00$; $chi^2 = 0.09$, df = 2 ($P = 0.96$); $I^2 = 0\%$						
Test for overall effect: $Z = 1.71$ ($P = 0.09$)						
Cases selected by 'non-favorable' fetal urinary biochemistry						
McLorie (2001)[26]	6	8	0	1	4.4	7.80 (0.23–262.81)
Freedman (1996)[25]	3	6	0	5	5.0	11.00 (0.43–284.30)
Johnson (1994)[24]	2	6	0	5	5.0	6.11 (0.23–162.73)
Crombleholme (1990)[21]	3	9	0	14	5.4	15.62 (0.70–348.11)
Subtotal (95% CI)		29		25	19.9	9.72 (1.89–50.09)
Total events	14		0			
Heterogeneity: $tau^2 = 0.00$; $chi^2 = 0.19$, df = 3 ($P = 0.98$); $I^2 = 0\%$						
Test for overall effect: $Z = 2.72$ ($P = 0.007$)						
Cases included with both 'favorable' and 'non-favorable' fetal urinary biochemistry						
Morris (2015)[27]	4	9	24	30	13.7	0.20 (0.04–0.98)
Morris (2013)[5]	9	13	3	13	12.3	7.50 (1.31–43.03)
Lipitz (1993)[23]	6	12	3	7	11.3	1.33 (0.20–8.71)
Nicolini (1991)[22]	2	6	0	7	5.0	8.33 (0.32–215.68)
Subtotal (95% CI)		40		57	42.3	1.71 (0.26–10.99)
Total events	21		30			
Heterogeneity: $tau^2 = 2.49$; $chi^2 = 10.46$, df = 3 ($P = 0.02$); $I^2 = 71\%$						
Test for overall effect: $Z = 0.56$ ($P = 0.57$)						
Total (95% CI)		112		134	100.0	2.54 (1.14–5.67)
Total events	64		52			
Heterogeneity: $tau^2 = 0.57$; $chi^2 = 14.99$, df = 10 ($P = 0.13$); $I^2 = 33\%$						
Test for overall effect: $Z = 2.28$ ($P = 0.02$)						
Test for subgroup differences: $chi^2 = 2.70$, df = 2 ($P = 0.26$), $I^2 = 25.8\%$						



Fetal surgical management: VAS

Survival at 6-12 months

Study	Intervention Events	Intervention Total	No intervention Events	No intervention Total	Weight (%)	Odds ratio M–H, random, 95% CI
Ruano (2015)[9]	7	13	12	35	29.4	2.24 (0.61–8.16)
Morris (2015)[27]	2	10	24	35	26.9	0.11 (0.02–0.63)
Morris (2013)[5]	8	14	2	14	26.1	8.00 (1.28–50.04)
Nicolini (1991)[22]	2	6	0	7	17.6	8.33 (0.32–215.68)
Total (95% CI)		43		91	100.0	1.77 (0.25–12.71)
Total events	19		38			

Heterogeneity: $tau^2 = 3.01$; $chi^2 = 13.44$, $df = 3$ ($P = 0.004$); $I^2 = 78\%$

Test for overall effect: $Z = 0.57$ ($P = 0.57$)

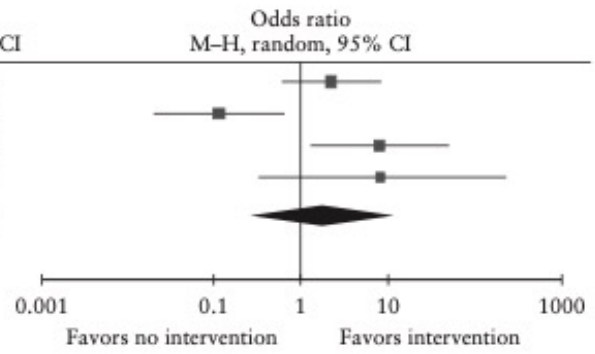


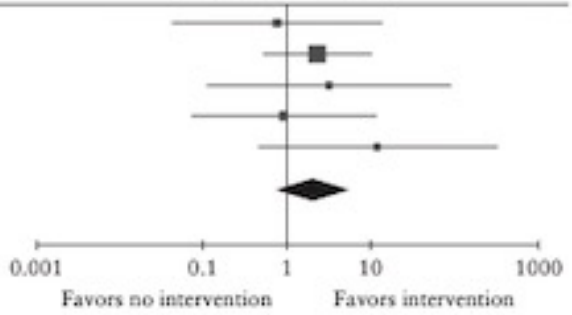
Figure 3 Forest plot of postnatal survival at 6–12 months of age in fetuses with lower urinary tract obstruction treated with vesicoamniotic shunt (intervention) or conservative management (no intervention). M–H, Mantel–Haenszel.

Postnatal kidney function

Study	Intervention Events	Intervention Total	No intervention Events	No intervention Total	Weight (%)	Odds ratio M–H, random, 95% CI
Morris (2015)[27]	1	2	13	23	13.0	0.77 (0.04–13.87)
Ruano (2015)[9]	6	10	11	28	50.0	2.32 (0.53–10.13)
Morris (2013)[5]	2	7	0	3	9.9	3.18 (0.12–87.92)
Freedman (1996)[25]	11	14	4	5	16.9	0.92 (0.07–11.58)
Crombleholme (1990)[21]	8	8	3	5	10.1	12.14 (0.46–323.23)
Total (95% CI)		41		64	100.0	2.09 (0.74–5.94)
Total events	28		31			

Heterogeneity: $tau^2 = 0.00$; $chi^2 = 2.06$, $df = 4$ ($P = 0.73$); $I^2 = 0\%$

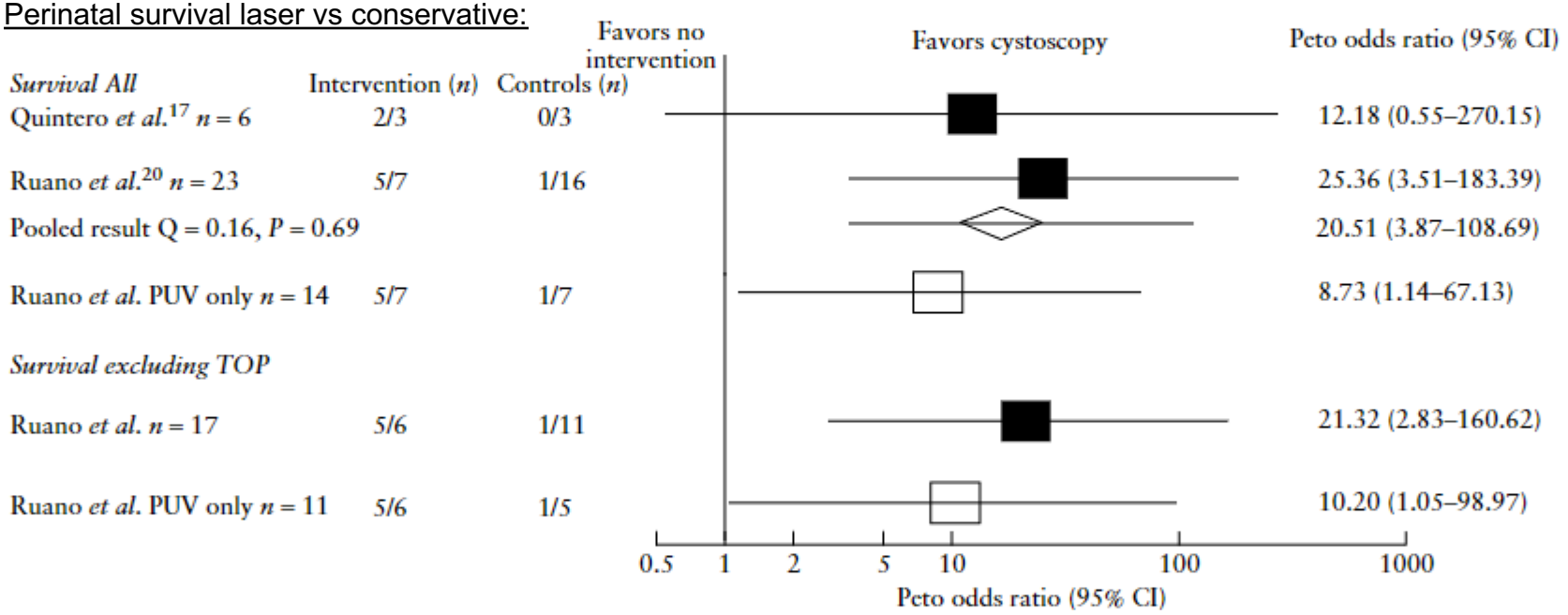
Test for overall effect: $Z = 1.39$ ($P = 0.17$)



Fetal surgical management cystoscopic laser ablation of PUVs

Metanalysis, 4 studies, 63 fetuses
VAS vs cystoscopic laser ablation of PUVs vs conservative management

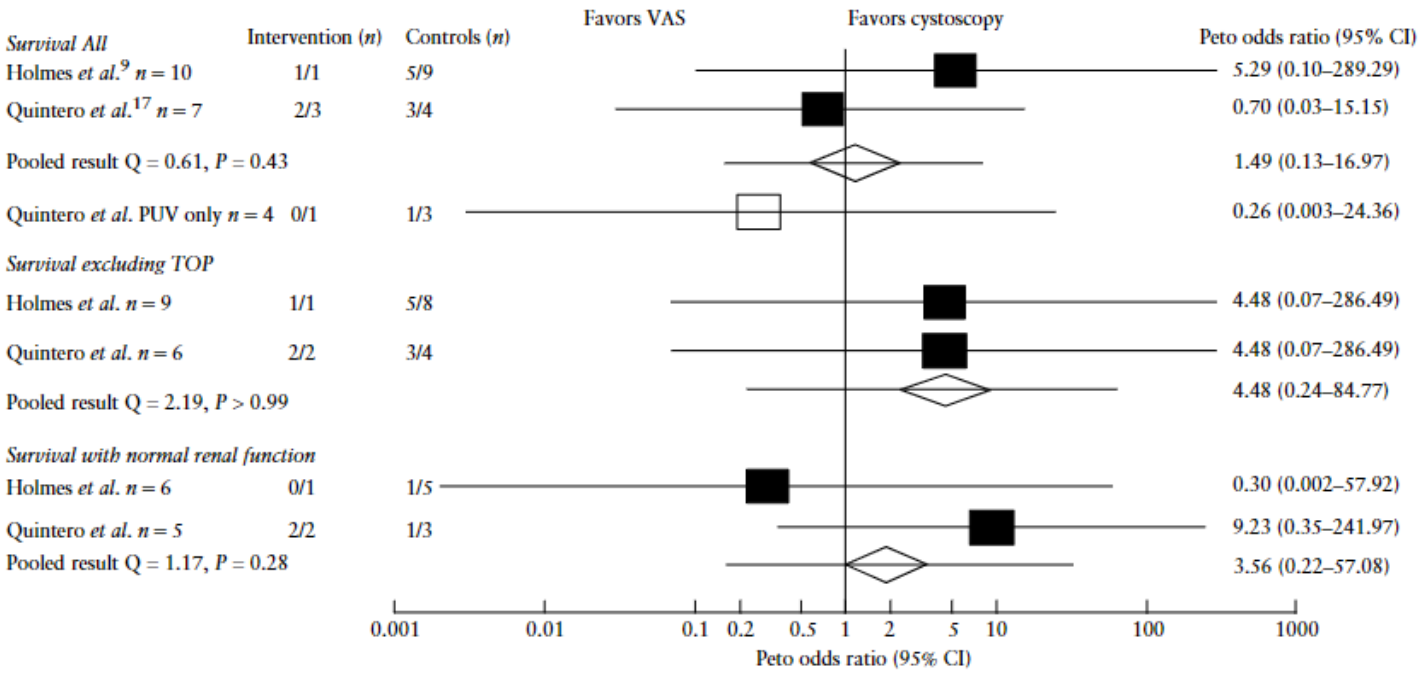
Perinatal survival laser vs conservative:



Morris RK, *Ultrasound Obstet. Gynecol, 2011*

Fetal surgical management cystoscopic laser ablation of PUVs

Perinatal survival laser vs VAS



Morris RK, *Ultrasound Obstet. Gynecol, 2011*

Fetal surgical management

Recommendation 7
Based on existing evidence that vesico-amniotic shunt placement increases perinatal survival in fetuses with LUTO, fetal intervention should be offered in selected cases. However, parents should be made aware of the residual risk of long-term mortality and kidney function impairment.

Conclusions

- Prenatal diagnosis, severity assessment and correct management of LUTO are challenging, given the lack of specific diagnostic features that can guide clinical approaches and decisions
- Fetuses with prenatal megacystis need to be referred to a tertiary obstetric centre with multidisciplinary expertise
- If prenatal treatment is indicated, parents must be informed about the potential benefits for postnatal survival, but they should also be made aware of the residual risk of postnatal kidney failure
- Further studies are needed to improve standardization of ultrasonographic diagnostic parameters, validate prenatal biomarkers and improve staging systems to optimize prenatal care and to provide a more accurate selection of patients who might benefit most from fetal intervention, in terms of long- term survival and kidney function.

THANK YOU!

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Aude Servais (Paris, France)

21/03/23

Glycogen storage disease Ib and XI, disease mechanisms and novel treatment
Francesco Trepiccione (Naples, Italy)

25/04/23

Disorders of renal calcium handling
Pascal Houillier (Paris, France)

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