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Fetal lower urinary tract obstruction: international Delphi consensus on management and core outcome set

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KEYWORDS: consensus; core outcome set; Delphi; LUTO; megacystis; obstructive uropathy; pregnancy

CONTRIBUTION

What are the novel findings of this work?
The most reliable method to assess renal function prognosis in fetal lower urinary tract obstruction (LUTO) is via imaging parameters of renal dysplasia, including cortical cysts and/or loss of corticomedullary differentiation. Fetal vesicocentesis to evaluate bladder refill or renal biochemistry can be used for prognostication and counseling. However, their role in assessing renal function and identifying candidates for fetal intervention is not clear. Vesicoamniotic shunt should be the first-line intervention for fetal LUTO and serial amnioinfusion should only be offered under research protocols. We developed a core outcome set and a workflow pathway for prenatal workup and management of LUTO.

What are the clinical implications of this work?
These consensus-based diagnostic criteria and management strategies should inform prospective studies to facilitate the evaluation of fetal LUTO using a consistent set of core outcomes. Our management pathway should be adopted into routine clinical practice and integrated into future guidance.

ABSTRACT

Objectives *To reach an international expert consensus on the diagnosis, prognosis and management of fetal lower urinary tract obstruction (LUTO) by means of a Delphi procedure, and to use this to define a core outcome set (COS).*

Methods *A three-round Delphi procedure was conducted among an international panel of experts in fetal LUTO. The panel was provided with a list of literature-based parameters to consider for the diagnosis, prognosis, management and outcomes of LUTO. A parallel procedure was conducted with patient groups during the development of the COS.*

Results *A total of 168 experts were approached, of whom 99 completed the first round and 80/99 (80.8%) completed all three rounds of the study questionnaires. Consensus was reached that, in the first trimester, an objective measurement of longitudinal bladder diameter of ≥ 7 mm should be used to suspect LUTO. In the second trimester, imaging parameters suggestive of LUTO could include enlarged bladder, keyhole sign, bladder wall thickening, bilateral hydronephrosis,*

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bilateral hydroureteronephrosis and male sex. There was 79% agreement that the current prognostic scoring systems in the literature should not be used clinically. However, experts agreed on the value of amniotic fluid volume (at < 24 weeks) to predict survival and that the value of fetal intervention is to improve the chance of neonatal survival. Experts endorsed sonographic parameters suggestive of renal dysplasia, at least one vesicocentesis, and renal biochemistry for prognosis and counseling, but these items did not reach a consensus for determining candidacy for fetal intervention. On the other hand, imaging parameters suggestive of LUTO, absence of life-limiting structural or genetic anomalies, gestational age of ≥ 16 weeks and oligohydramnios (defined as deepest vertical pocket < 2 cm) should be used as candidacy criteria for fetal intervention based on expert consensus. If bladder refill was evaluated, it should be assessed subjectively. Vesicoamniotic shunt should be the first line of fetal intervention. In the presence of suspected fetal renal failure, serial amnioinfusion should be offered only as an experimental procedure under research protocols. A COS for future LUTO studies was agreed upon.

Conclusion *International consensus on the diagnosis, prognosis and management of fetal LUTO, as well as the COS, should inform clinical care and research to optimize perinatal outcomes. © 2024 The Author(s). Ultrasound in Obstetrics & Gynecology published by John Wiley & Sons Ltd on behalf of International Society of Ultrasound in Obstetrics and Gynecology.*

INTRODUCTION

Congenital lower urinary tract obstruction (LUTO) refers to a heterogeneous group of anatomical abnormalities that cause an obstruction at the level of the fetal urethra[1]. The most common cause of LUTO is posterior urethral valves, which occur almost exclusively in male fetuses, in approximately 2.1 per 10 000 live births[2,3].

LUTO varies in etiology and severity and may result in a sequence of prenatal events that are detectable on ultrasonographic evaluation. LUTO is usually associated initially with a distended bladder (megacystis) and is often accompanied by progressive hydroureter and hydronephrosis. Later in gestation, fetuses may develop abnormal renal parenchymal appearance[4]. In severe cases, LUTO eventually results in the early onset of oligohydramnios or anhydramnios, resulting in pulmonary hypoplasia and neonatal death[5]. Of the patients who survive, up to 30% develop end-stage renal disease, requiring dialysis and renal transplantation by the age of 5 years[6].

Prenatal intervention for LUTO, primarily using vesicoamniotic shunt placement, has been advocated based on the rationale that restoring normal amniotic fluid volume by shunting fetal urine from the obstructed urinary system to the amniotic space prevents pulmonary hypoplasia and, thus, improves neonatal survival. This was shown in the PLUTO trial, the only randomized clinical trial comparing the effectiveness of expectant management *vs* vesicoamniotic shunting[7]. However, data regarding candidacy for fetal surgery for LUTO and its outcomes remain limited.

In 2018, the European Reference Network for Rare Kidney Diseases (ERKNet) established a working group to develop a consensus regarding the diagnosis and management of LUTO[8]. Although this publication provided guidance for some aspects of prenatal diagnosis, many questions related to prognosis, candidacy for surgical intervention, outcomes and procedural details were left unanswered.

In addition, the lack of consistency in reported LUTO outcomes results in substantial reporting bias and an inability to synthesize homogeneous results across studies in systematic reviews. This problem could be addressed using a core outcome set (COS), which is currently not available for LUTO. A COS is a set of critical outcomes that should be measured and reported, as a minimum, in a standardized manner in future studies on that topic[9].

We established a working group with the aim of reaching a consensus on the approach to prenatal LUTO diagnosis and management, and to develop a COS for prenatally diagnosed LUTO that incorporates the views of key stakeholders, including health professionals, researchers and those personally affected by LUTO.

METHODS

Delphi design

The Delphi methodology was used, in which a series of structured statements are scored and revised, fed back to the participants and repeated in multiple rounds, in increasing detail, until consensus has been reached[10]. This procedure aims to refine the opinions of participating experts while minimizing confounding factors that are present in other group-response methods[11]. The rationale for its use is that it is a well-established instrument used to reach a consensus within an expert panel on research questions that cannot be answered with empirical evidence and complete certainty.

Participants provided informed consent before commencement of the first round of the study, and were reminded of their right to anonymity and the ability to withdraw before each subsequent round.

Core outcome set

The development of a COS was planned per the methodology recommended in the Core Outcome Measures in Effectiveness Trials (COMET) handbook version 1.0[9] and by the International Consortium for Health Outcomes Measurement[12], and drew upon the experience of the core steering group in developing other COS in the field of women's health. This study was registered in the COMET database (registration number: 2079) and further details are available at https://www.comet-initiative.org/Studies/Details/2079.

Panel selection

Experts were considered eligible for participation if they satisfied at least one of the following inclusion criteria: expertise in fetal LUTO, based on a relevant publication record identified through a systematic review to identify research gaps for the fetal LUTO Delphi consensus, during which authors of relevant publications were extracted; membership of a pertinent scientific organization, including the North American Fetal Therapy Network (NAFTNet), International Fetal Medicine and Surgery Society (IFMSS) or International Society for Prenatal Diagnosis (ISPD); and recommendation for participation by another invitee, based on relevant expertise in fetal LUTO. Key stakeholder groups included general obstetricians, maternal–fetal medicine specialists, neonatologists, pediatric urologists and nephrologists, and patient groups affected by LUTO. Patients with a history of fetal LUTO, and their parents and caregivers, were invited to participate in the development of the COS. Potential participants were sent an invitational e-mail detailing the inclusion criteria.

Systematic review

The design and methods of the systematic review complied with the guidance of the Centre for Reviews and Dissemination (CRD) for undertaking reviews in healthcare[13] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement[14]. The protocol of this study was registered in PROSPERO (registration number: CRD42023428303).

A comprehensive search strategy (Appendix S1) was employed by two independent authors (H.J.M. and A.A.N.), who inputted combinations of the relevant Medical Subject Headings (MeSH) terms and keywords into MEDLINE, EMBASE, Scopus, CINAHL and CENTRAL, from inception until June 2022. A manual search was also conducted to identify any missed publications.

The search included all studies reporting ultrasound findings, management and outcomes of fetuses with hydronephrosis, hydroureteronephrosis and/or megacystis with prenatally suspected and/or postnatally confirmed LUTO. Randomized controlled trials, cohort studies and case series were included. Surveys, commentaries, case reports and studies without the full text available were excluded. Review articles were excluded after cross-referencing with the collected studies to ensure the inclusion of other potentially relevant citations. Full-text articles were screened by two independent authors (H.J.M. and A.N.N.) to confirm eligibility based on the inclusion and exclusion criteria.

First round

Based on the results of the systematic review, four domains were used to structure the first round of the Delphi study and were presented to the expert panel: (1) 'prenatal ultrasonographic parameters to diagnose fetal LUTO and its workup', comprising topics such as sonographic features for prenatal suspicion of LUTO in the first and second trimesters, timing of diagnosis, diagnostic parameters for megacystis and additional tests; (2) 'prediction of renal function and survival in fetuses with LUTO', addressing the use of sonographic and biochemical parameters to predict renal function and survival; (3) 'fetal intervention for prenatally suspected LUTO', covering indications, timing and methods of fetal surgical intervention and delivery; and (4) 'core outcome set' for reporting fetal LUTO.

Response options included multiple choice answers or a five-point Likert scale (5, strongly agree; 1, strongly disagree). A predefined cut-off for group consensus on an item or group of similar answers was ≥ 70% agreement[15]. Items with 60–69% agreement were reconsidered in the next round, while < 60% agreement reflected a lack of consensus and items were not considered in the following rounds, unless it was felt that rewording was necessary. Participants were able to provide feedback or suggest additional items in each round, which was used by the core steering group to adjust items.

Second and third rounds

Items that reached consensus in the first round were presented to the expert panel for confirmation in the second round. Items with significant agreement (60–69% agreement) were reconsidered following rephrasing of the question-and-answer options, or with a new question added to provide clarification. Items with < 60% agreement were presented for confirmation of exclusion. The third round applied the same protocol as the second, with the additional goal to synthesize and reach a consensus on the final core items from each domain.

A separate, two-round, parallel Delphi procedure was conducted for the experts and patient/patient representative group to provide perspectives for consideration in the COS. The same set of core outcomes was presented, and participants were also able to suggest new outcomes. Following the finalization of items in the third round, both outcome sets were merged and presented to all participants for final agreement.

Data collection and analysis

Data were collected in three consecutive rounds using online questionnaires that were presented to panelists through a unique token-secured link for each round. Responses were captured in REDCap version 13.7.19 (Vanderbilt University, Nashville, TN, USA). Non-responders received e-mail reminders after 2 and 4 weeks and were excluded from subsequent rounds if no response was received. Each round included the option of offering additional items or suggestions, as well as withdrawal of items from the survey. Newly suggested items were categorized and considered carefully by the expert panel for their applicability in this process. Experts' demographic details were collected, including country, age, years of experience, specialty, practice type

and setting, LUTO-related publications, number of fetal and pediatric LUTO assessments performed, number of fetal and pediatric LUTO intervention procedures conducted and practiced fetal intervention types, if any. Data analysis was performed using Excel Workbook and results were presented in frequency tables.

RESULTS

Systematic review search

In total, 37 190 records were identified in the systematic review search. Following abstract screening, 646 full-text articles were assessed for eligibility. After full-text review, 46 articles were included. A PRISMA flowchart is provided in Figure S1.

Participants

A total of 168 experts were identified and invited to participate. Of these, 99 completed the first round and 80/99 (80.8%) completed all three rounds. Nine women with a previous pregnancy complicated by LUTO participated in the development of the COS. The demographic and clinical characteristics of the experts are described in Table 1. On average, experts were ≥ 45 years of age and had a predominantly Western geographical distribution, including Europe and North America. In addition, 70.7% were from obstetric/gynecological specialties and subspecialties and 26.3% were pediatric urologists, pediatric nephrologists or neonatologists.

The most common category for the number of pregnancies receiving assessment for fetal LUTO per year at the experts' institutions was 5–14 (46.1% of experts), and the most common category for the number of pregnancies requiring LUTO intervention assessment per year at their institution was fewer than five (48.1% of experts). Moreover, 76.1% of experts reported fewer than five deliveries at their institution following shunt placement; however, the number of pediatric LUTO cases managed was higher (70.3% reported 5–24 cases). The type of fetal intervention offered at the experts' institutions was most commonly vesicoamniotic shunting only (74.2%), followed by both shunt and cystoscopy (9.7%) and cystoscopy only (3.2%).

Sonographic parameters for detection and workup of suspected fetal LUTO

Eighteen ultrasound signs for detection of fetal LUTO were identified in the systematic review (Appendix S2). Delphi findings regarding first- and second-trimester ultrasound signs and level of agreement per round are outlined in Table 2.

In the first trimester, consensus was reached that megacystis should be assessed with a combination of subjective and objective measures, but evaluation should be predominantly objective using specific ultrasonographic measurements (88.7% agreement). A longitudinal bladder diameter (LBD) of ≥ 7 mm measured from superior to inferior in the sagittal plane should be used to suspect and monitor for possible LUTO (88.7% agreement). A LBD of ≥ 15 mm, with a bladder that fails to empty, is strongly suggestive of a LUTO diagnosis and is unlikely to resolve (90.3% agreement). Although LUTO can be suspected in the first trimester, it is optimally diagnosed from at least 16 weeks' gestation (98.4% agreement). Experts agreed (75.8%) that a first-trimester echocardiogram should be used to rule out associated cardiac anomalies only if the institution has the relevant resources to conduct and interpret first-trimester echocardiography; otherwise, mid-trimester echocardiography should be performed. In addition, experts agreed (96.8%) that nuchal translucency should be assessed.

In the second trimester, consensus was reached that the objective bladder-size formulae proposed by Fontanella *et al.*[16] and Maizels *et al.*[17] to define an enlarged bladder should not be used clinically (87.1% agreement). Although it did not reach a consensus, there was significant agreement (64.5%) that an enlarged bladder in the second trimester should be assessed in a predominantly subjective manner for failure to void throughout the ultrasound scan, with no particular time limit. Consensus was also not reached on the proposed definition by Fontanella *et al.*[18] of failure to void over 40 min. Oligohydramnios can be determined beyond 16 weeks' gestation, at which point it should be predominantly assessed objectively (90.3% agreement) using deepest vertical pocket (DVP) < 2 cm as the first-line criterion (100% agreement), while the amniotic fluid index (AFI) < 5th percentile and < 5 cm should not be used as first-line diagnostic criteria for oligohydramnios (88.7% agreement). Experts agreed that the presence of the following parameters should be suggestive of obstructive (i.e. LUTO) rather than non-obstructive causes of enlarged bladder: enlarged bladder (assessed subjectively), keyhole sign, bladder wall thickening (assessed subjectively), bilateral hydronephrosis, bilateral hydroureteronephrosis, and male sex in addition to all of the above parameters (87.1% agreement). Our Delphi study did not investigate the definition and classification of hydronephrosis, as this was already addressed by the ERKNet group[8].

Experts agreed that the following parameters are not required for the diagnosis of LUTO: urinoma, urinary ascites, echogenic kidney, renal cortical cysts, loss of corticomedullary differentiation, gestational age (GA) at diagnosis and renal agenesis (85.5% agreement). All experts agreed (100%) that diagnostic genetic evaluation should be offered, and first-line testing should be either chorionic villous sampling (CVS) or amniocentesis (95.2% agreement), while genetic testing obtained via vesicocentesis or cordocentesis should not be used as first-line testing (85.5% agreement). The genetic samples should be sent primarily for fluorescence *in-situ* hybridization or polymerase chain reaction and microarray (96.8% agreement), while other investigations, including exome sequencing and syndromic panels, might be considered

Table 1 Demographic and baseline characteristics of experts on fetal lower urinary tract obstruction (LUTO) who completed first round of Delphi process

Characteristic	*Respondents* (n = *99*)
Age*	
25–44 years	27/97 (27.8)
45–54 years	33/97 (34.0)
≥ 55 years	37/97 (38.1)
Region of practice	
UK	35 (35.4)
USA	29 (29.3)
Netherlands	13 (13.1)
France	6 (6.1)
Canada	6 (6.1)
Italy	3 (3.0)
Other†	7 (7.0)
Specialty	
Obstetrics and gynecology	70 (70.7)
Fetal medicine	66 (66.7)
General obstetrics and gynecology	3 (3.0)
Maternal–fetal medicine	2 (2.0)
Pediatrics	29 (29.3)
Pediatric urology	17 (17.2)
Pediatric nephrology	8 (8.1)
Neonatology	1 (1.0)
Other	3 (3.0)
Academic rank	
Professor	38 (38.4)
Specialist/consultant	36 (36.4)
Associate/assistant professor	21 (21.2)
Other	4 (4.0)
Practice setting	
University academic hospital-based practice	96 (97.0)
Private practice	2 (2.0)
Community academic hospital-based practice	1 (1.0)
Years in practice	
≤ 9 years	19 (19.2)
10–19 years	38 (38.4)
≥ 20 years	42 (42.4)
Published papers on fetal LUTO	62 (62.6)
Principal investigator; first, second or last author	48 (48.5)
Number of LUTO assessments at expert's institution per annum*	
< 5	11/89 (12.4)
5–14	41/89 (46.1)
15–34	31/89 (34.8)
≥ 35	6/89 (6.7)
Number of intervention assessments for fetal LUTO at expert's institution per annum*	
< 5	39/81 (48.1)
5–14	31/81 (38.3)
15–34	10/81 (12.3)
≥ 35	1/81 (1.2)
Number of pregnancies that required LUTO intervention delivered at expert's institution per annum*	
None	23/96 (24.0)
1–4	50/96 (52.1)
5–34	23/96 (24.0)
Number of pediatric LUTO cases managed at expert's institution per annum*	
< 5	13/74 (17.6)
5–24	52/74 (70.3)
≥ 25	9/74 (12.2)
Fetal intervention procedures offered at expert's institution*	
Vesicoamniotic shunt only	46/62 (74.2)
Cystoscopy only	2/62 (3.2)
Both vesicoamniotic shunt and cystoscopy	6/62 (9.7)
None	8/62 (12.9)

Data are given as *n*/*N* (%) or *n* (%). *Data missing as some experts declined to answer. †Brazil, Croatia, Belgium, Hong Kong, Mexico, Turkmenistan or Ireland.

Table 2 Ultrasonographic parameters for the detection and workup of fetal lower urinary tract obstruction (LUTO) considered by expert panel in three Delphi rounds

Parameter	*Round 1 (n = 70)*	*Round 2 (n = 62)*	*Round 3 (n = 60)*
First trimester			
Megacystis assessment			
Objective (ultrasonography) only	27 (38.6)	—	—
Subjective (bladder prominence) only	5 (7.14)	—	—
Both objective and subjective	38 (54.3)	—	—
Both objective and subjective, but predominantly objective	—	55 (88.7)	—
LBD cut-off			
≥ 7 mm to suspect and monitor for possible LUTO	54 (77.1)	55 (88.7)	—
≥ 12 mm to suggest diagnosis of LUTO, with a bladder that fails to empty	26 (37.1)	6 (9.7)	—
≥ 15 mm to suggest diagnosis of LUTO, with a bladder that fails to empty	40 (57.1)	56 (90.3)	—
Use of echocardiography to rule out associated cardiac anomalies, if institution has resources	40 (57.1)	47 (75.8)	—
Assessment of nuchal translucency	66 (94.3)	60 (96.8)	—
Optimal GA for LUTO diagnosis			
≥ 14 weeks	27 (38.6)	—	—
≥ 16 weeks	30 (42.9)	61 (98.4)	—
≥ 18 weeks	7 (10.0)	—	—
Second trimester			
Enlarged bladder assessment			
Objective (ultrasonography) only	11 (15.7)	—	—
Subjective (bladder prominence) only	23 (32.9)	—	—
Both objective and subjective	34 (48.6)	—	—
Both objective and subjective, but predominantly subjective	—	40 (64.5)	—
Enlarged bladder definitions to be used clinically			
Enlarged bladder that fails to void over a period of 40 min during ultrasonographic examination with no standardized measurement cut-offs[18]	28 (40.0)	—	—
Predicted LBD = GA in weeks − 5[17]	9 (12.9)	—	—
PUV LBD *Z*-score > 5.2 is complex megacystis[16]	9 (12.9)	—	—
LBD between GA + 2 and GA + 12 is suggestive of PUV while beyond that suggests complex megacystis[17]	7 (10.0)	—	—
Predicted LBD = 1.48 × GA − 17.15[16]	7 (10.0)	—	—
None of the above definitions	—	54 (87.1)	—
Objective assessment should not be used	40 (57.1)	—	—
Oligohydramnios assessment			
Objective	34 (48.6)	—	—
Deepest vertical pocket < 2 cm	56 (80.0)	62 (100)	—
AFI < 5th percentile	18 (25.7)	—	—
AFI < 5 cm	16 (22.9)	—	—
Neither AFI < 5th percentile nor < 5 cm should be used	—	55 (88.7)	—
Subjective	3 (4.3)	—	—
Both objective and subjective	33 (47.1)	—	—
Predominantly objective, with a degree of subjective	—	56 (90.3)	—
Parameters suggestive of obstructive rather than non-obstructive cause of enlarged bladder			
Keyhole sign	65 (92.9)	—	—
Oligohydramnios or anhydramnios	65 (92.9)	—	—
Enlarged bladder	56 (80.0)	—	—
Bladder wall thickening	54 (77.1)	—	—
Bilateral hydronephrosis	51 (72.9)	—	—
Bilateral hydroureteronephrosis	49 (70.0)	—	—
All of the above	—	59 (95.2)	—
Consideration of male sex with above parameters	47 (67.1)	54 (87.1)	—
Parameters not predominantly required for LUTO diagnosis			
Urinoma or urinary ascites	37 (52.9)	—	—
Echogenic kidney	40 (57.1)	—	—
Cortical cysts	47 (67.1)	—	—
Loss of corticomedullary differentiation	49 (70.0)	—	—
GA at diagnosis	55 (78.6)	—	—
Renal agenesis	70 (100)	—	—
None of the above is required	—	53 (85.5)	—

Continued over.

Table 2 *Continued*

Parameter	*Round 1 (n = 70)*	*Round 2 (n = 62)*	*Round 3 (n = 60)*
Diagnostic genetic testing			
Should be offered	68 (97.1)	62 (100)	—
Methods of sample collection			
CVS	61 (87.1)	—	—
Amniocentesis	59 (84.3)	—	—
Either CVS or amniocentesis	—	59 (95.2)	—
Vesicocentesis	28 (40.0)	—	—
Cordocentesis	17 (24.3)	—	—
Neither bladder vesicocentesis nor cordocentesis	—	53 (85.5)	—
Amnioinfusion then amniocentesis	13 (18.6)	—	—
First-line laboratory tests to order			
FISH (or PCR) and microarray	54 (77.1)	60 (96.8)	—
Exome sequencing	26 (37.1)	—	—
Overgrowth syndromic panel	4 (5.71)	—	—
Neither exome sequencing nor overgrowth syndromic panel as first line, but may be considered later	—	48 (77.4)	—
Fetal MRI is recommended but not compulsory in suspected LUTO	—	40 (64.5)	56 (93.3)

Data are given as *n* (%). Items in this domain were not displayed to pediatric experts ($n = 29$). Consensus was defined as ≥ 70% agreement, significant agreement as 60–69% and no agreement as < 60%. —, Item not addressed in round; AFI, amniotic fluid index; CVS, chorionic villus sampling; FISH, fluorescence *in-situ* hybridization; GA, gestational age; LBD, longitudinal bladder diameter; MRI, magnetic resonance imaging; PCR, polymerase chain reaction; PUV, posterior urethral valves.

later (77.4% agreement). Experts agreed (93.3%) that fetal magnetic resonance imaging (MRI) is encouraged, but not compulsory, in cases where LUTO is suspected.

Recommendations

- In the first trimester, LUTO should be suspected through a predominantly objective assessment of the fetal bladder, using a LBD of ≥ 7 mm. A LBD of ≥ 15 mm, with a bladder that fails to empty, is strongly suggestive of a LUTO diagnosis and is unlikely to resolve.
- In the first trimester, fetal echocardiography should be offered only if institutional resources and expertise are available.
- LUTO can be optimally diagnosed only from at least 16 weeks' gestation.
- In the second trimester, the combination of the following can be suggestive of obstructive rather than non-obstructive uropathy: male sex, enlarged bladder (assessed subjectively), keyhole sign, bladder wall thickening (assessed subjectively), bilateral hydronephrosis and bilateral hydroureteronephrosis. However, urinoma, urinary ascites, echogenic kidney, cortical cysts, loss of corticomedullary differentiation, GA at diagnosis and renal agenesis are not required for the diagnosis.
- In the second trimester, for suspected LUTO, the following workup should be offered: comprehensive anatomy scan, fetal echocardiography, and diagnostic genetic testing primarily via CVS or amniocentesis (vesicocentesis and cordocentesis should not be used for first-line testing). Offering fetal MRI is encouraged but not compulsory.
- Oligohydramnios should be primarily diagnosed using DVP < 2 cm, after 16 weeks' gestation.
- Genetic testing should primarily include fluorescence *in-situ* hybridization or polymerase chain reaction and microarray. Exome sequencing and syndromic panels can be used in secondary workup.

Prediction of renal function and survival in fetuses with LUTO

The results of the systematic review for workup and suggested scoring or staging systems for fetal LUTO are outlined in Appendix S3. Delphi findings regarding the prediction of renal function and survival and the agreement level for each round are outlined in Table 3.

To predict renal function, consensus was reached that sonographic imaging findings that are highly suggestive of renal dysplasia include renal cortical cysts (90.0% agreement), loss of corticomedullary differentiation (81.4% agreement), and unilateral or bilateral subjectively assessed echogenic kidneys (75.7% agreement), whereas the presence of anhydramnios, oligohydramnios, urinoma or ascites is not suggestive of renal dysplasia (80.6% agreement). For further evaluation of renal dysplasia, vesicocentesis should be considered (85.5% agreement), with at least one vesicocentesis procedure performed (93.5% agreement), primarily to evaluate bladder refill (82.3% agreement) and renal biochemistry (85.5% agreement), but not to relieve urinary pressure (88.7% agreement). If a second vesicocentesis is performed, then renal biochemistry can be assessed (91.9% agreement), and the parameters that reached consensus were sodium level (normal cut-off < 100 mmol/L) (82.9% agreement) and β_2-microglobulin level (normal cut-off < 6 mg/dL) (80.0% agreement), whereas other biochemical parameters did not reach consensus (osmolality had 68.6% agreement; calcium,

Table 3 Parameters for prediction of renal function and survival in fetuses with lower urinary tract obstruction (LUTO) considered by expert panel in three Delphi rounds

Parameter	*Round 1 (n = 70)*	*Round 2 (n = 62)*	*Round 3 (n = 60)*
Prediction of renal function			
Renal dysplasia ultrasound parameters to be used			
Renal cortical cysts	63 (90.0)	—	—
Loss of corticomedullary differentiation	57 (81.4)	—	—
Unilateral or bilateral echogenic kidneys	53 (75.7)	—	—
All of the above should be used	—	61 (98.4)	—
Renal dysplasia ultrasound parameters not to be used			
Anhydramnios	29 (41.4)	—	—
Oligohydramnios	43 (61.4)	—	—
Urinoma or ascites	61 (87.1)	—	—
None of the above should be used	—	50 (80.6)	—
Vesicocentesis should be considered in LUTO workup	47 (67.1)	53 (85.5)	—
To assess renal biochemistry	54 (77.1)	53 (85.5)	—
To consider assessment of bladder refill	44 (62.9)	51 (82.3)	—
Not to relieve renal pressure	56 (80.0)	55 (88.7)	—
Number of vesicocentesis procedures			
Depends on the results	23 (32.9)	—	—
One	16 (22.9)	—	—
Two	20 (28.6)	—	—
Three	7 (10.0)	—	—
At least one	—	58 (93.5)	—
Bladder refill evaluation for LUTO intervention candidacy			
Subjective assessment	41 (58.6)	37 (59.7)	42 (70.0)
Objective: > 80% urine volume on the tap	17 (24.3)	—	—
Objective: > 50% urine volume on the tap	13 (18.6)	25 (40.3)	—
Objective assessment	—	—	8 (13.3)
Both subjective and objective assessment	—	—	10 (16.7)
Renal biochemistry			
Assessment			
By vesicocentesis	45 (64.3)	57 (91.9)	—
By cordocentesis	2 (2.9)	—	—
By vesicocentesis or cordocentesis (depending on feasibility)	13 (18.6)	—	—
Parameters			
Sodium (normal cut-off < 100 mmol/L)	58 (82.9)	—	—
β_2-microglobulin (normal cut-off < 6 mg/L)	56 (80.0)	—	—
Osmolality (normal cut-off < 200 mOsm/L)	48 (68.6)	—	—
Chloride (normal cut-off < 90 mOsm/L)	40 (57.1)	—	—
Calcium (normal cut-off < 8 mg/L)	37 (52.9)	—	—
Total protein (normal cut-off < 20 mg/dL)	15 (21.4)	—	—
Peptidome (12PUV) expression	4 (5.7)	—	—
Biochemistry should be used as a prognostic factor	—	48 (77.4)	—
Prenatal LUTO staging criteria			
Ruano (2016)[21]	34 (48.6)	—	—
Fontanella (2019)[20]	20 (28.6)	—	—
Nassr (2021)[19]	17 (24.3)	—	—
None of the above	—	49 (79.0)	—
New prenatal staging system	41 (58.6)	48 (77.4)	—
Prediction of survival			
Likelihood of fetal or neonatal survival can be foreseen prenatally	62/99 (62.6)	60/82 (73.2)	—
Best indicator is amniotic fluid at < 24 gestational weeks	86/99 (86.9)	77/82 (93.9)	—
Risk of postnatal renal replacement therapy or transplant cannot be foreseen prenatally, in the absence of imaging suggestive of renal dysplasia	39/99 (39.4)	63/82 (76.8)	—
Value of fetal intervention is to improve survival	—	64/82 (78.0)	69/80 (86.3)
No strong evidence of improvement of renal function after fetal intervention in LUTO	—	61/82 (74.4)	79/80 (98.8)

Data are given as *n* (%) or *n/N* (%). Items in this domain were not displayed to pediatric experts, except for those relating to prediction of survival. Consensus was defined as ≥ 70% agreement, significant agreement as 60–69% and no agreement as < 60%. —, Item not addressed in round; 12PUV, 12-peptide signature.

chloride, total protein and peptidome (12PUV) expression had < 60% agreement).

Experts agreed (76.8%) that, in the absence of imaging findings suggestive of renal dysplasia, the risk of postnatal renal replacement therapy or transplant cannot be foreseen prenatally.

The scoring and staging systems for fetal LUTO proposed by Nassr *et al.*[19], Fontanella *et al.*[20] and Ruano *et al.*[21] should not be adopted into clinical practice at present (79.0% agreement).

Experts agreed (73.2%) that the likelihood of fetal or neonatal survival can be foreseen prenatally, and the best indicator of survival is the amniotic fluid volume before 24 weeks' gestation (93.9% agreement).

Recommendations

- The most reliable method to predict renal function is using imaging parameters of renal dysplasia, including renal cortical cysts, loss of corticomedullary differentiation, and unilateral or bilateral subjectively assessed echogenic kidneys (presence of anhydramnios, oligohydramnios, urinoma or ascites are not suggestive of renal dysplasia).
- To further assess for renal dysplasia, at least one vesicocentesis procedure should be considered, primarily to assess bladder refill for prognosis and counseling.
- Vesicocentesis should not be primarily used to assess renal biochemistry or to relieve renal pressure.
- If more than one vesicocentesis is performed, renal biochemistry can be tested to aid prognosis and counseling.
- The likelihood of fetal or neonatal survival could be foreseen prenatally, with the best indicator being the amniotic fluid volume before 24 weeks' gestation.
- In the absence of imaging findings suggestive of renal dysplasia, the risk for postnatal renal replacement therapy or transplants cannot be foreseen prenatally.
- None of the scoring and staging systems proposed in the literature should be adopted clinically yet.

Fetal intervention for prenatally suspected LUTO

Appendix S4 outlines the systematic review data compiled regarding fetal intervention for LUTO, including candidacy, timing and type of intervention. Table 4 outlines Delphi findings regarding fetal intervention, including the level of agreement in each round.

Intervention candidacy

Once imaging is suggestive of LUTO (as outlined above), experts agreed that the inclusion criteria for intervention should include absence of life-limiting genetic or structural anomalies, reduced amniotic fluid volume (oligohydramnios or anhydramnios) and gestational age of at least 16 weeks (93.5% agreement). The characterization of life-limiting genetic or structural anomalies should be individualized based on the multidisciplinary managing team's discussion.

No consensus was reached on whether bladder refill should be used to determine intervention candidacy (53.3% stated it should not be used). However, experts agreed that if bladder refill evaluation was used for LUTO intervention candidacy, it should be assessed subjectively (70.0% agreement) (Table 3). No consensus was reached for the objective methods of bladder refill assessment proposed in the literature, including those of Ruano *et al.*[21,22] (< 27% reduction in volume 48 h after vesicocentesis) and Nassr *et al.*[19] (volume at 48 h after vesicocentesis ≥ 80% of initial volume), in determining eligibility for intervention. Although there was no consensus, there was significant agreement (63.3%) that renal biochemistry parameters should not be used to assess for LUTO intervention candidacy (Table 4). Consensus was not reached regarding whether the presence of ultrasonographic features suggestive of renal dysplasia should be used as an exclusion criterion for intervention (53.3% agreement that it should not be used). Although there was no consensus, there was significant agreement (62.9%) that shunt intervention should be considered for female fetuses with presumed LUTO.

Intervention timing

Experts agreed (88.7%) that the minimum GA for intervention is 16 weeks. Although there was no consensus, there was significant agreement (64.5%) that 28 weeks should be the maximum GA at which first-time fetal shunt intervention is offered. Experts agreed (96.8%) that re-shunting for a displaced shunt should be considered, even at an advanced preterm GA. Experts agreed (86.3%) that the value of fetal intervention is to improve the chance of perinatal survival (Table 3).

Intervention type

Experts agreed (91.9%) that vesicoamniotic shunt should be the primary intervention offered for fetal LUTO (Table 4). Experts also agreed that peritoneal–amniotic shunt placement, cystoscopic valve fulguration, serial amnioinfusion, transurethral stent placement or ultrasound-guided balloon catheterization should not be offered as first-line intervention (87.1% agreement). There was consensus (88.7%) that, in the presence of suspected fetal renal failure, serial amnioinfusion should only be offered under Institutional Review Board research protocols, such as the Renal Anhydramnios Fetal Therapy (RAFT) Trial[23] (NCT03101891), the methodology of which experts emphasized as the suggested technique. Opinions on the technique of vesicoamniotic shunting were not sought given the variability of available shunt types across countries.

Recommendations

- The value of fetal intervention is to improve the chance of perinatal survival.

Table 4 Parameters for fetal intervention in prenatally suspected lower urinary tract obstruction (LUTO) considered by expert panel in three Delphi rounds

Parameter	*Round 1 (n = 70)*	*Round 2 (n = 62)*	*Round 3 (n = 60)*
Criteria to use for fetal intervention candidacy			
Absence of life-limiting genetic abnormalities	57 (81.4)	—	—
Absence of life-limiting structural anomalies	56 (80.0)	—	—
GA of at least 16 weeks	46 (65.7)	—	—
Oligohydramnios	40 (57.1)	—	—
Anhydramnios	31 (44.3)	—	—
All of the above	—	58 (93.5)	—
Criteria not to use for fetal intervention candidacy			
Prognostic parameters based on renal biochemistry	31 (44.3)	—	38 (63.3)
Presence or absence of seal of CAS (regardless of GA)	39 (55.7)	—	38 (63.3)
Bladder refill	31 (44.3)	—	32 (53.3)
Ultrasound features suggestive of renal dysplasia	35 (50.0)	—	32 (53.3)
None of the above should be used	—	36 (58.1)	—
Minimum GA at which to offer fetal intervention of first shunt			
16 weeks	45 (64.3)	55 (88.7)	—
14 weeks	6 (8.6)	—	—
Any GA in the absence of CAS	10 (14.3)	—	—
Maximum GA at which to offer fetal intervention of first shunt			
24 weeks	22 (31.4)	—	—
28 weeks	22 (31.4)	40 (64.5)	—
30 weeks	2 (2.9)	—	—
32 weeks	16 (22.9)	—	—
Re-shunting for a displaced shunt should be considered at a later gestation	50 (71.4)	60 (96.8)	—
Shunting should be considered for presumed LUTO in female fetus	34 (48.6)	39 (62.9)	—
Vesicoamniotic shunt should be the primary intervention offered in LUTO	62 (88.6)	57 (91.9)	—
Interventions not to be offered as first-line for LUTO			
Peritoneal–amniotic shunt	50 (71.4)	—	—
Cystoscopic valve fulguration	53 (75.7)	—	—
Cystoscopic transurethral stent placement	62 (88.6)	—	—
Both of the above	60 (85.7)	—	—
Serial amnioinfusion	58 (82.9)	—	—
Ultrasound-guided balloon catheterization	62 (88.6)	—	—
None of the above should be offered as first-line	—	54 (87.1)	—
In the presence of renal failure, serial amnioinfusion should not be offered, unless under research protocol	50 (71.4)	55 (88.7)	—

Data are given as *n* (%). Consensus was defined as ≥ 70% agreement, significant agreement as 60–69% and no agreement as < 60%.
—, Item not addressed in round; CAS, chorioamniotic separation; GA, gestational age.

- Inclusion criteria for fetal LUTO intervention are imaging suggestive of LUTO, absence of life-limiting genetic or structural anomalies, reduced amniotic fluid volume (oligohydramnios or anhydramnios) and gestational age of at least 16 weeks.
- Bladder refill and renal biochemistry can be used as part of LUTO workup for prognosis and counseling, but their role in intervention candidacy is not clear.
- Although imaging should be used to assess renal dysplasia for prognosis and counseling, its role as an exclusion criterion for intervention, if dysplasia was suspected, is not clear.
- There is significant agreement, but not consensus, that the maximum GA at first-time shunt intervention is 28 weeks, whereas re-shunting after displacement of a shunt can be considered at a later GA.
- There is significant agreement, but not consensus, that intervention should be considered for female fetuses with presumed LUTO.
- Vesicoamniotic shunt should be the primary intervention offered in fetal LUTO.
- Serial amnioinfusion should be offered only under research protocols.
- The decision for delivery mode and timing should follow routine obstetric indications and recommendations.

Although 77.4% of experts agreed that a new prenatal staging system for LUTO should be devised, it was not feasible to do so based on the results of this Delphi procedure because of a lack of consensus on some intervention candidacy exclusion criteria. However, a management workflow was generated based on the results (Figure 1).

Core outcome set for future fetal LUTO studies

A final list of antenatal, procedure-related, survival and postnatal study outcomes was agreed upon by healthcare and patient group experts (Table 5). These were classified as core or relevant outcomes to account for feasibility in future trials. The majority of experts agreed that all future fetal LUTO studies should cover long-term outcomes (95.1% agreement).

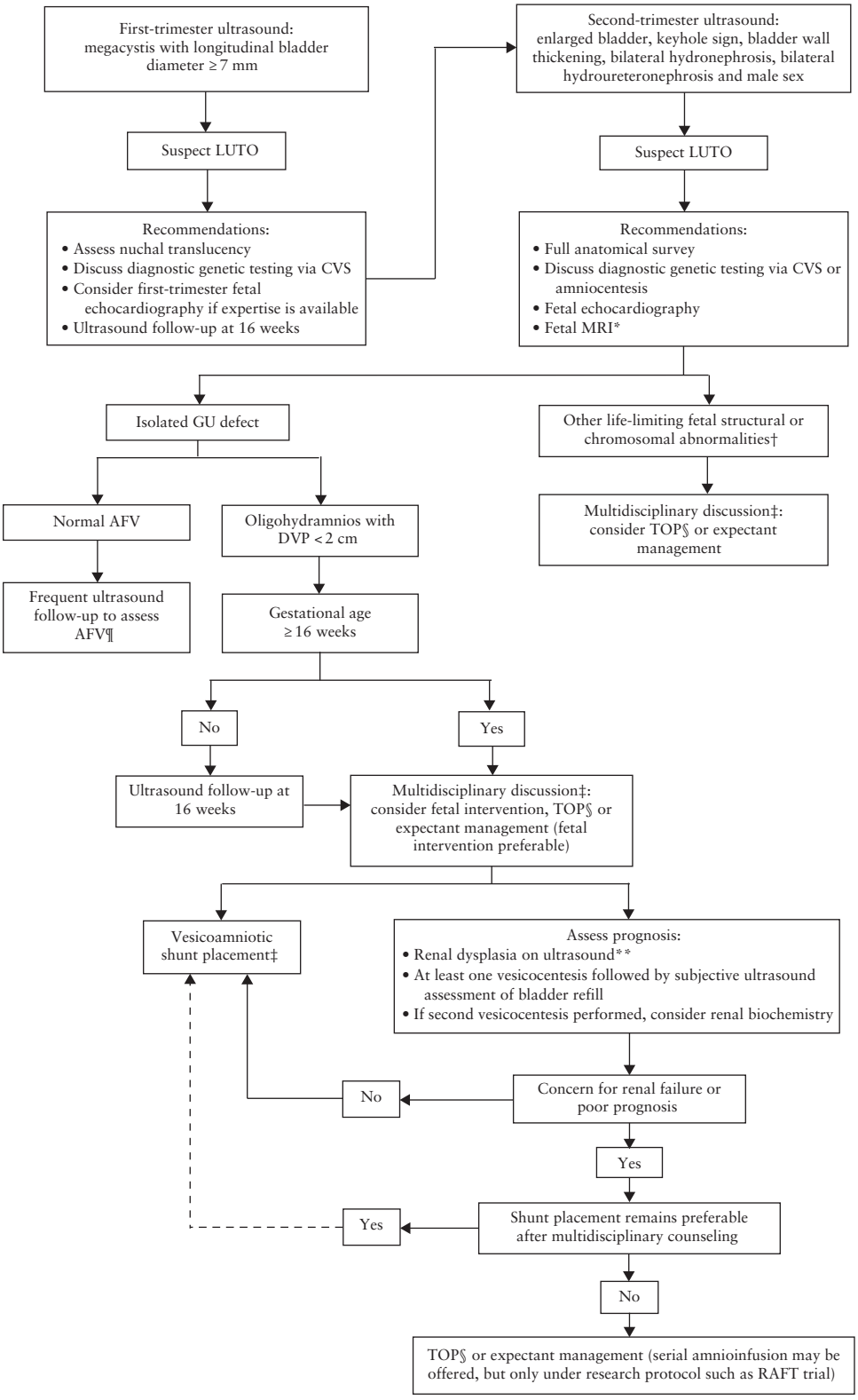

Figure 1 Flowchart summarizing Delphi-generated workflow pathway for diagnosis and management of fetal lower urinary tract obstruction (LUTO). *Experts agreed it should be considered but is not compulsory. †No specific diagnoses were assessed in Delphi procedure; life-limiting impression is made following multidisciplinary discussion. ‡Multidisciplinary discussion including experts in fetal medicine, neonatology, urology and nephrology, in addition to patients and others. §Considering country or state laws. ¶Frequency of assessment was not evaluated as part of Delphi procedure; however, authors perform weekly assessment. **Experts agreed that presence of any of the following could be indicative of renal dysplasia: cortical cysts, loss of corticomedullary differentiation, unilateral or bilateral subjectively assessed echogenic kidneys. Dashed line indicates that, although experts agreed to use outlined methods to assess for prognosis and counseling, no agreement was reached to use them for fetal intervention candidacy. AFV, amniotic fluid volume; CVS, chorionic villous sampling; DVP, deepest vertical pocket; GU, genitourinary; MRI, magnetic resonance imaging; RAFT, Renal Anhydramnios Fetal Therapy; TOP, termination of pregnancy.

Table 5 Delphi consensus-derived core outcome set for fetal lower urinary tract obstruction (LUTO)

Parameter	*Round in which consensus was reached (% agreement)*	*Category of outcome*
Survival outcomes		
Intrauterine fetal death	3 (96.3)	Core
Live birth	3 (96.3)	Core
Perinatal survival	3 (96.3)	Core
Neonatal survival	3 (96.3)	Core
One year of survival	3 (96.3)	Core
Two years of survival	3 (92.5)	Relevant
Five years of survival	3 (92.5)	Relevant
Survival to hospital discharge	3 (92.5)	Relevant
Termination of pregnancy	3 (92.5)	Relevant
Miscarriage	3 (92.5)	Relevant
Spontaneous preterm birth	3 (92.5)	Relevant
Prenatal and perinatal outcomes		
Ultrasonographic appearance of kidneys	3 (97.5)	Core
Amniotic fluid deepest vertical pocket	3 (97.5)	Core
Gestational age at delivery	3 (97.5)	Core
Progression/resolution of megacystis	3 (95.0)	Relevant
Preterm delivery (< 32 weeks)	3 (95.0)	Relevant
Chorioamnionitis	3 (95.0)	Relevant
PPROM	3 (95.0)	Relevant
Procedure-to-delivery interval	3 (95.0)	Relevant
Procedure-related outcomes		
Fetal complications (organ injury, bladder rupture, abdominal wall defect)	3 (100)	Core
Fetal death within 1 week after procedure	3 (100)	Core
Maternal complications (organ injury, infection, bleeding)	3 (100)	Core
PPROM within 7 days after procedure	3 (100)	Core
Failed shunt insertion	3 (100)	Core
Shunt dislodgment or blockage	3 (100)	Core
Fetal death beyond 1 week after procedure	3 (86.3)	Relevant
Chorioamniotic separation	3 (86.3)	Relevant
Neonatal outcomes		
Need for kidney replacement therapy	3 (95.0)	Core
Need for peritoneal dialysis or hemodialysis	3 (95.0)	Core
Pulmonary hypoplasia	3 (95.0)	Core
Intubation and conventional mechanical ventilation, high-frequency ventilation or jet ventilation	3 (95.0)	Core
Posterior urethral valve with or without requirement of a procedure	3 (95.0)	Core
Pulmonary hypertension	3 (95.0)	Core
Renal biochemistry, creatinine and GFR levels (at day 3, 1 month and before discharge)	3 (95.0)	Core
Birth weight	3 (86.3)	Relevant
Respiratory distress syndrome	3 (86.3)	Relevant
Neonatal intensive care unit admission	3 (86.3)	Relevant
Prematurity-related outcomes (intraventricular hemorrhage, leukomalacia, retinopathy, necrotizing enterocolitis)	3 (86.3)	Relevant
Requirement for vesicostomy	3 (86.3)	Relevant
Length of hospital stay	3 (86.3)	Relevant
Requirement for primary endoscopic valve ablation	3 (86.3)	Relevant
Urosepsis	3 (86.3)	Relevant
Apgar score	3 (86.3)	Relevant
Number of operative postnatal procedures	3 (86.3)	Relevant
Pathological hydroureter or hydronephrosis	3 (86.3)	Relevant
Urinary ascites	3 (86.3)	Relevant
Joint contractures	3 (86.3)	Relevant
Long-term outcomes		
Renal transplant	3 (98.7)	Core
Chronic kidney disease and staging	3 (98.7)	Core
Need for urinary diversion procedures (vesicostomy, ureterostomy, nephrostomy or suprapubic bladder catheterization)	3 (98.7)	Core
Neurodevelopmental outcomes	3 (98.7)	Core
Need for nephrectomy	3 (89.9)	Relevant
Need for augmentation procedures	3 (89.9)	Relevant
Need for bladder neck procedures for continence	3 (89.9)	Relevant
Need for anti-reflux procedure (endoscopic or open)	3 (89.9)	Relevant
Psychosocial factors	3 (89.9)	Relevant
Need for repeat valve resection	3 (89.9)	Relevant
Need for bladder and bowel medication	3 (89.9)	Relevant

Some outcomes were classed as relevant (significant but not an essential component to all trials) to account for feasibility in future trials.
GFR, glomerular filtration rate; PPROM, preterm prelabor rupture of membranes.

DISCUSSION

Summary of findings

In this three-round Delphi procedure, including 99 multidisciplinary stakeholders from 13 countries across four continents, we reached a consensus on criteria for prenatal diagnosis, investigation and intervention in fetal LUTO, and developed a COS for reporting LUTO. Additionally, we were able to generate a prenatal management workflow.

Interpretation of key findings

Regarding diagnosis of fetal LUTO, the agreement to use DVP rather than AFI in diagnosing oligohydramnios is consistent with the literature, which shows that use of AFI results in overdiagnosis[24,25]. The ERKNet group[8] agreed on using the anteroposterior diameter of the renal pelvis to assess for hydronephrosis, as proposed by the Urinary Tract Dilation (UTD) classification[26]. Although we identified objective assessments for enlarged bladder in the literature, including the proposals by Fontanella *et al.*[16] and Maizels *et al.*[17], no consensus was reached and, until further evidence can be gathered, experts agreed on using subjective assessment to diagnose enlarged bladder.

Regarding identified prenatal workup, the recommendation for fetal echocardiography is in line with the literature, which shows an increased association of congenital heart diseases with renal anomalies[27]. This is also in line with the American Heart Association (AHA)[28] and American Institute of Ultrasound in Medicine (AIUM)[29], which recommend fetal echocardiography if extracardiac anomalies are seen. The role of fetal MRI lies mainly in the differentiation of complex urogenital pathologies, assessing renal parenchymal differentiation and thickness, and assessing for extrarenal anomalies. There are some data that fetal MRI may provide reliable renal functional information[30]. Regarding diagnostic genetic testing, the experts agreed that first-line testing should be through CVS or amniocentesis, and not through vesicocentesis, as the latter is less likely to obtain enough fetal DNA.

Regarding prognosis, data in the literature are limited and unvalidated. Proposed methods to assess prognosis that were presented to the panel included ultrasonographic imaging suggestive of renal dysplasia[4], bladder refill assessment using vesicocentesis[21] and renal biochemistry[31]. The group of experts did not agree with the proposals for objective assessment for bladder refill suggested in the literature, including that of Ruano *et al.*[21,22] who suggested $<27\%$ volume reduction 48 h after vesicocentesis, and that of Nassr *et al.*[19], who suggested bladder tap volume $>80\%$ of the initial volume 48 h after vesicocentesis. However, it was agreed that bladder refill should be assessed subjectively, which will evidently lead to interobserver variability. The role of renal biochemistry has remained controversial in the literature for three main reasons: large margins of uncertainty, the lack of homogeneity in cases selected and diversity in the management of cases tested prenatally. A meta-analysis by Morris *et al.*[32] of 23 studies identified three biochemical markers that were considered to be associated with renal function, namely calcium, sodium and β_2-microglobulin, but with low sensitivity and specificity. Additionally, Klein *et al.*[33] used proteomics to identify 30 fetal urinary peptides that can be used to determine the prognosis of postnatal renal function in posterior urethral valves. However, this promising method cannot yet be used routinely and was not agreed upon by the expert panel.

Regarding candidacy for fetal intervention, the ERKNet group did not offer relevant information[8]. The PLUTO trial criteria included singleton male fetuses, imaging suggestive of LUTO and absence of major genetic or structural anomalies, but no limit was determined for gestational age or amniotic fluid volume[7]. Although our expert panel agreed upon the criteria for intervention, they did not agree on whether poor prognosis diagnosed with sonographic imaging, bladder refill or renal biochemistry would be part of the exclusion criteria for intervention, which is mostly related to the controversy and lack of strong evidence on the role of these methods. This represents a knowledge gap that needs to be addressed in future studies. Although there was consensus that vesicoamniotic shunting was the primary prenatal therapeutic intervention, there are several different types of shunt available that might affect efficacy[34,35]. Shunt choice should aim to maximize successful insertion while minimizing complications of shunt blockage and displacement, as well as minimizing rupture of membranes, for which there are currently efforts to create new shunts with improved characteristics[36,37]. Intervention has been shown to improve perinatal survival rather than renal function, but this information is based on the PLUTO trial, which had a small sample size and was conducted over a decade ago. New multicenter studies to address this issue are warranted.

Strengths and limitations

The strengths of our study include the use of the well-established Delphi procedure and the inclusion of a diverse group of international experts. Before generating our Delphi questionnaire, we conducted a thorough systematic review of the literature to identify every aspect of investigation in this field and present it to our stakeholders. Our preselection criteria for participation, based on clinical and academic experience, resulted in a high degree of expertise among our panel, including mostly obstetric or pediatric seniors with either a publication on the topic or exposure through working in specialized fetal centers. Moreover, a low attrition rate was seen across the three rounds. We were able to generate a clinically informative flowchart based on our results, which provides a practical guide and builds on current knowledge gaps regarding management protocols for fetal LUTO. Another major strength is the use of validated consensus-building methodology, incorporating Delphi and nominal group techniques to converge many potential outcomes into a focused, clinically important

set of core outcomes. This should facilitate not only the collection of real-world evidence for the assessment of treatment efficacy, but it could also serve as a useful tool for shared decision-making and treatment assessment.

A limitation of our study is that the Delphi output reflects a current interpretation of existing literature, which can change over time. As a summary of expert opinions, it also constitutes a lower level of research evidence than a prospective study design. Additionally, given the presentation of consensus results in follow-up rounds, participants may have altered their initial thoughts to prioritize the consensus views to strengthen group unanimity[38]. This was minimized by masking individual expert opinions that could steer the group in a particular direction, adding relevant questions raised by individual participants guided by a working group, and the independent nature of the questionnaire itself.

Similar to other international Delphi studies, there was underrepresentation from countries in South America and Africa, which could be explained by the topic constituting a lower research priority or the lack of availability of fetal LUTO interventions in these regions, compared with Europe and North America.

Conclusions and future implications

We propose that our consensus-based diagnostic criteria and management pathway should be integrated into standard clinical practice to facilitate the evaluation of fetal LUTO. Gaps remain regarding intervention exclusion criteria, alternative therapies, if any, and definition for diagnosis of renal failure. Although we addressed prenatal genetic testing methodologies, we did not address different genetic diagnoses and their implications on LUTO outcome, and the role of prenatal intervention remains unknown. Future studies should either validate existing prognostic methods or investigate novel methodologies for evaluation of renal function. Studies should also assess outcomes using different forms of intervention, different shunts, and the role of early GA at intervention on survival and renal function prognosis. Furthermore, these methods should be incorporated into the fetal intervention candidacy model to evaluate their effectiveness in determining ideal candidates for intervention. Our COS should be incorporated into future studies to standardize outcomes, particularly when reporting long-term outcomes, given the paucity of data in this population.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Figure S1 PRISMA flowchart for the search and selection process.

Appendix S1 Systematic review search strategy

Appendix S2 Summary of 18 ultrasound signs for detection of fetal lower urinary tract obstruction (LUTO) suggested in literature and number of studies they are reported in

Appendix S3 Proposed workup, staging, and scoring systems suggested in literature for suspected fetal lower urinary tract obstruction (LUTO)

Appendix S4 Systematic review data regarding parameters for candidacy for intervention, timing and type of intervention

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Obstrucción fetal del tracto urinario inferior: consenso Delphi internacional sobre el tratamiento y el conjunto básico de resultados

RESUMEN

Objetivos. Alcanzar un consenso internacional de expertos sobre el diagnóstico, el pronóstico y el tratamiento de la obstrucción fetal del tracto urinario inferior (OTUI) mediante un procedimiento Delphi, y utilizarlo para definir un conjunto básico de resultados (CBR).

Métodos. Se llevó a cabo un procedimiento Delphi de tres rondas entre un panel internacional de expertos en OTUI fetal. Se proporcionó al grupo de expertos una lista de parámetros basados en la bibliografía que debían tenerse en cuenta para el diagnóstico, el pronóstico, el tratamiento y los resultados del OTUI. Durante el desarrollo del CBR se llevó a cabo un procedimiento paralelo con grupos de pacientes.

Resultados. Se contactó un total de 168 personas expertas, de las cuales 99 completaron la primera ronda y 80 de las 99 (80,8%) completaron las tres rondas de cuestionarios del estudio. Se llegó al consenso de que, en el primer trimestre, debería utilizarse una medición objetiva del diámetro longitudinal de la vejiga de ≥7 mm para sospechar una OTUI. En el segundo trimestre, entre los parámetros de las imágenes que podrían sugerir una OTUI podrían estar una vejiga agrandada, signo del ojo de cerradura, engrosamiento de la pared vesical, hidronefrosis bilateral, hidroureteronefrosis bilateral y sexo masculino. Hubo un 79% de acuerdo en que los sistemas actuales de puntuación para pronóstico en la bibliografía no deberían utilizarse clínicamente. Sin embargo, los expertos coincidieron en el valor del volumen de líquido amniótico (a <24 semanas) para predecir la supervivencia y en que el valor de la intervención fetal es mejorar la probabilidad de supervivencia neonatal. Los expertos respaldaron los parámetros ecográficos que sugieren displasia renal, al menos una vesicocentesis y la bioquímica renal para el pronóstico y el asesoramiento, pero estos elementos no alcanzaron un consenso para determinar candidatos a intervención fetal. Por otro lado, los parámetros de las imágenes que podrían sugerir OTUI, la ausencia de anomalías estructurales o genéticas incapacitantes, la edad gestacional ≥16 semanas y el oligohidramnios (definido como cavidad vertical más profunda <2 cm) deben utilizarse como criterios de candidatura para la intervención fetal basados en el consenso de expertos. Si se evalúa el llenado vesical, debería hacerse de forma subjetiva. La derivación vesicoamniótica debe ser la primera opción de intervención fetal. Si se sospecha una insuficiencia renal en el feto, la amnioinfusión seriada sólo debería ofrecerse como procedimiento experimental en el marco de protocolos de investigación. Se acordó un CBR para estudios futuros sobre OTUI.

Conclusión. El consenso internacional sobre el diagnóstico, pronóstico y manejo de la OTUI fetal, así como el CBR, debe asesorar la atención clínica y la investigación para optimizar los resultados perinatales.

胎儿下尿路梗阻：关于管理和核心结果集的国际德尔菲共识

摘要

目的 通过德尔菲程序就胎儿下尿路梗阻（LUTO）的诊断、预后和管理达成国际专家共识，并以此定义核心结果集（COS）。

方法 由国际胎儿下尿路梗阻专家组成的专家组进行了三轮德尔菲程序。专家小组获得了一份基于文献的参数清单，用作 LUTO 的诊断、预后、管理和结果参考。在制定 COS 的过程中，还与患者组进行了平行程序。

结果 共接触了 168 名专家，其中 99 人完成了第一轮问卷调查，80/99（80.8%）人完成了全部三轮问卷调查。专家们一致认为，在孕早期，客观测量膀胱纵向直径≥7 毫米即可怀疑 LUTO。在孕中期，提示 LUTO 的影像学参数可包括膀胱增大、钥匙孔征、膀胱壁增厚、双侧肾积水、双侧输尿管积水性肾病和男性。79% 的专家一致认为，目前文献中的预后评分系统不应在临床上使用。然而，专家们一致认为羊水量（<24 周时）对预测存活率有价值，胎儿干预的价值在于提高新生儿存活率。专家们认可提示肾脏发育不良的声像图参数、至少一次膀胱穿刺术和肾脏生化检查对预后和咨询的作用，但这些项目并未就确定胎儿干预的候选资格达成共识。另一方面，根据专家共识，提示 LUTO 的影像学参数、无危及生命的结构或遗传异常、胎龄≥16 周和羊水过少（定义为最深垂直袋<2 厘米）应作为胎儿干预的候选标准。如果要评估膀胱充盈情况，则应主观评估。膀胱羊膜腔分流术应作为胎儿干预的首选方案。在出现疑似胎儿肾功能衰竭的情况下，只有在研究方案下作为实验性程序才能进行连续羊膜腔灌注。专家组还就未来 LUTO 研究的 COS 达成了共识。

结论 关于胎儿 LUTO 的诊断、预后和管理的国际共识以及 COS，应为临床护理和研究提供依据，以优化

围产期结局。