SFM Fetal Therapy Practice Guidelines: Fetal Cystoscopic Laser Ablation

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Abstract

Fetal lower urinary tract obstruction (LUTO) in a male fetus could cause detrimental effects to the KUB (kidney, ureter, and bladder) system from back-pressure changes as well as to the lungs from reduced amniotic fluid. In a carefully selected case where the obstruction causes progressive damage, a therapeutic intervention could be lifesaving. In utero vesico-amniotic shunting has been shown to improve perinatal pulmonary survival, but evidence on improvement of renal outcomes with this procedure is lacking. More recently, fetal cystoscopic laser fulguration has been shown to be beneficial in longer-term survival and renal outcomes. These interventions carry significant risk, and therefore patient selection and optimal timing are key. This guideline lists the intricacies of patient selection, relevant counseling points and procedural details.

Keywords
- LUTO
- PUV
- fetal cystoscopy
- laser fulguration

Indication

Fetal lower urinary tract obstruction (LUTO) in a male fetus due to presumed posterior urethral valve (PUV) with oligo or anhydramnios and salvageable renal parameters (LUTO stage II, Ruano staging; ►**Table 1**), preferably with good bladder refilling after a bladder tap, in a singleton pregnancy with normal karyotype and no additional fetal malformation.[1]

Fetoscopic laser ablation may be indicated if the following conditions are fulfilled[2]:

- The etiology of LUTO is PUV.
- Oligohydramnios/anhydramnios.

A favorable Urine analysis report on sequential bladder sampling (suggestive of preserved renal function) is considered ideal, but not mandatory.[3]

Contraindications

- Female fetus.
- Presence of an irregular, lobulated, and folded nondistended megabladder (suggestive of a primary prune-belly syndrome).
- Absence of keyhole sign.
- Sonologic features suggestive of renal dysplasia/in utero renal failure such as and cortical cysts with echogenic stroma and no or poor (<27%) bladder refilling after vesicocentesis.[1]
- Presence of other systemic malformations or genetic abnormalities.

Maternal Risks

Maternal risks are rare, with incidence lower than 1 in 1,000. Possible risks include the following:

- Injury to bowel or bladder/viscera.
- Injury to the inferior epigastric vessels leading to rectus sheath hematoma.
- Injury to the superficial branches of the uterine artery leading to hemoperitoneum.

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Table 1 Staging of LUTO (Based on Ruano staging)

Stage	Bladder	Kidneys	Liquor	Urine biochemical analysis	Bladder refill	Verdict
Stage 1	Distended	B/l HUN	Normal	Favorable	Good	Mild LUTO
Stage 2	Distended	Echogenic kidneys w/o cortical cysts	Starts to decrease or oligoamnios	Favorable	Good	Severe LUTO Preserved renal function
Stage 3	Distended	Echogenic kidneys with cortical cysts	Severe oligo- or anhydramnios	Poor	Minimal	Severe LUTO Abnormal renal function
Stage 4	Distended/ collapsed	Dysplastic kidneys	Anhydramnios	Poor	Nil or <27%	In utero renal failure

Abbreviations: B/l, bilateral; HUN, hydroureteronephrosis; LUTO, lower urinary tract obstruction; w/o, without.

Fetal Risks

- Recurrence of obstruction (20%).
- Urorectal or vesicocutaneous fistula (13%).
- Need for repeat procedure with either cystoscopy or vesico-amniotic shunting (VAS) placement (10%).
- Preterm premature rupture of membranes.
- Rarely, fetal demise.

Patient Information Leaflet

1. What is LUTO?
   LUTO refers to an outflow obstruction to urine at the level of the bladder outlet. Hence, it is also referred to as bladder outlet obstruction (BOO).
2. What is a PUV?
   A PUV is an extra flap of fetal tissue that is in the urethra. The urethra is the tube that carries urine from the bladder out of the body. They are the most common cause of LUTO detected during the antenatal and immediate postnatal period in male fetuses, with a reported incidence of 1 in 5,000 live births. They account for at least 70 to 80% of all causes of LUTO, the remainder being made up by urethral atresia or stenosis. PUV causes problems to the fetus as it blocks the urine flow from the bladder, leading to retention of urine in the bladder and increased back pressure in the baby's kidneys. This leads to swelling of the entire urinary system and ultimately may damage the kidneys' irreversibly. From around the 16th week of pregnancy, the fluid that surrounds the baby (amniotic fluid) is predominantly the baby's urine. So, when there is a LUTO, the baby is unable to pass urine into the amniotic cavity and therefore the amount of amniotic fluid around the baby is reduced. In severe cases, there may not be any fluid left around it. As the baby's growth (especially lung growth and maturation) needs an adequate amount of fluid around it, in such a condition, this may be hampered.[4]
3. What causes PUV?
   PUV usually occurs by chance. It is not the result of anything that a mother did or did not do during pregnancy. Rarely, it could be associated with an underlying genetic disorder.
4. When is PUV diagnosed?
   Usually, this condition is diagnosed during a routine antenatal ultrasound at around 19 to 20 weeks of pregnancy (anomaly scan). In severe cases, it may be suspected or diagnosed earlier. This condition is suspected when there is a reduced amount of fluid around the baby and the scan shows an overdistended bladder and urethra. This implies that there is an obstruction to the flow of urine out of the bladder. A single scan may not be sufficient to diagnose this condition and serial ultrasonography may be required to confirm the diagnosis. However, ultrasonography alone is not sufficient for diagnosis. A final diagnosis can be made only after birth by several investigations. Before birth, an invasive diagnostic test called fetal cystoscopy may help confirm the diagnosis.
5. What are the signs and symptoms of PUV?
   Before birth, the ultrasonography findings that help diagnose this condition are the following:
   - Reduced or absent liquor amnii.
   - Distended bladder with a "keyhole" sign.
   - The entire urinary system may appear swollen depending on the degree and duration of the blockage of the urine flow (►**Fig. 1**).
   - After birth, the baby may show several symptoms like the following:
     - Repeated urinary tract infections.
     - Difficult urination, painful urination, or a weak urine stream.
     - Difficulty in breathing (due to associated lung hypoplasia).
     - Poor growth and slow development.
     - High blood pressure.
     - Difficulty in toilet training.
     - Bedwetting accidents longer than usual.
6. What are the medical complications of PUV?
   Some children born with partial PUV, or a less severe form of obstruction, may not have serious complications from PUV. However, children with severe PUV could have the following[5]:

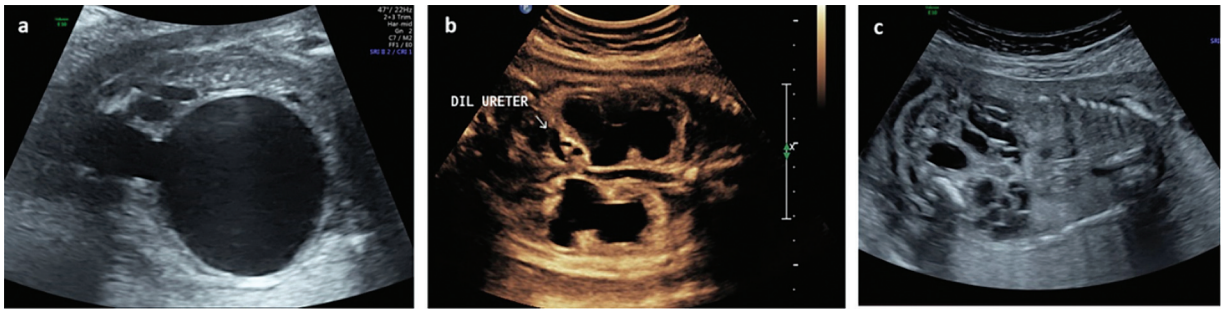

Fig. 1 Characteristic ultrasound features of lower urinary tract obstruction (LUTO): overdistended, thick-walled bladder with (**a**) the "keyhole" sign, (**b**) bilateral hydroureteronephrosis, and (**c**) oligohydramnios.

- Loss of kidney function and an inability to make normal urine.
- Bladder dysfunction.
- Severe hydronephrosis (swelling of the kidneys).
- Breathing problems due to immature lungs.
- Vesicoureteral reflux (backflow of urine from the bladder to the kidneys).

Some babies with PUV develop a condition called kidney failure. This can occur before the child is born, during the first few weeks of life, or in later life. When this happens, the child will need dialysis or a kidney transplant. Timely and proper bladder management may help slow down or prevent kidney failure.

7. How is PUV treated?
   After the baby is born, a pediatric surgeon/urologist can remove the PUV by one of several surgical techniques. However, if the bladder damage before birth, it could cause lifelong problems requiring regular follow-up with the doctor.[6] Before the birth of the baby, two treatment options are available:
   - Cystoscopic laser fulguration of the PUV: In this surgery, a laser fiber is passed through a metallic tube (-fetoscope/cystoscope) through the mother's abdomen, the baby's abdomen, and then into the baby's bladder.[7] The PUV is ablated/burnt using a laser. After successful ablation, the urinary block is relieved, leading to an unobstructed flow of urine into the baby's sac. This condition also relieves the back pressure on the kidneys, preventing any further damage. Also, the continuous urine stream ensures good bladder cycling and a good amount of fluid around the baby.
   - VAS: A coiled tube is passed into the baby's bladder, one end of which stays inside the bladder and the other end is brought out into the baby's amniotic sac.[8] It creates an alternate channel for urine flow, bypassing the block at the level of the urethra. This redirects urine into the baby's sac and, thus, increases the fluid around the baby.
8. If I choose to undergo surgery before birth, which surgical procedure is better?
   With current available evidence, cystoscopic laser ablation may have advantages over VAS[9] because of the following:
   - It allows visualization of the back part (posterior) of the urethra and may diagnose PUV as well as differentiate between PUV and other causes of BOO such as urethral atresia, which are not amenable to treatment.
   - It avoids frequent repeated surgeries that may often be necessary with shunting because the shunt may be displaced.
   - It may have the potential to allow a more physiological release of the obstruction and drainage as this is directed at mitigating the cause of the obstruction rather than creating a bypass channel.
9. What are the complications of such a procedure?
   Maternal complications are rare (<1/1,000) and could include the following:
   - Injury to the bowel or bladder/viscera.
   - Injury to the inferior epigastric vessels, leading to rectus sheath hematoma.
   - Injury to the superficial branches of the uterine artery leading to the hemoperitoneum.

   The following fetal complications are reported:
   - Recurrence of obstruction (20%).
   - Urorectal or vesicocutaneous fistula (13%).
   - Need for repeat procedure with either cystoscopy or VAS placement (10%).
   - Premature rupture of membranes.
   - Rarely, fetal demise.
10. If I undergo surgery before birth, does that mean that my baby can avoid all complications related to LUTO?
    Surgical procedures or interventions on your unborn child in such a condition are aimed at gaining maximum benefit by early intervention before the kidneys are irreversibly damaged. However, despite this proof of principle, the long-term benefits of such intervention are yet to be well studied. Some fetuses may not survive despite the intervention and those that do may still be at risk of increased neurological morbidity. Recent evidence quotes a 55% chance of live birth. None of the babies treated successfully had lung issues, 40% of fetuses treated and 73% of liveborn babies had normal renal function at 15 to 110 months, and only 3% had renal failure.

Counseling Statement for Medical Records

Detailed ultrasonographic evaluation of the fetus revealed findings consistent with LUTO, likely due to a posterior

urethral valve. The findings noted were bilateral hydroureteronephrosis, overdistended, thickened bladder, and the "keyhole"' sign suggestive of a proximal urethral dilatation. No other structural anomaly could be detected during the scan.

- The decreasing trend of amniotic fluid volume is suggestive of BOO coupled with progressive obstructive uropathy.
- The renal parenchyma appears nondysplastic by ultrasound at present, which may be suggestive of preserved/salvageable renal function.
- The renal function needs to be determined by serial vesicocentesis and urinary biochemical analysis.
- If serial vesicocentesis reveals favorable urine biochemical analytes, a cystoscopy-guided confirmation of the valve and its subsequent ablation using a laser may be considered.
- Fetal cystoscopy improves the 6-month survival rate in cases of severe LUTO and may prevent impairment of renal function in fetuses with PUV.

Consent

I, ……., & my husband/family member …… (name and relation) have understood the condition (LUTO) that my unborn baby is suffering from, in detail. The expected progression of the problem, its likely consequences, & complications thereof as well as the various management options that are available to us at this gestational age were explained. The possible fetal interventions with the pros and cons of each and the costs involved were also discussed in detail. We understand that fetal interventions for this condition do not guarantee a cure and my baby is likely to need additional procedures postnatally. All possible complications to the mother and fetus were also explained in detail and include preterm delivery, premature membrane rupture, bleeding, infection, miscarriage, fetal demise, recurrence of the fetal problem, and need for reinterventions. We understand that the procedure will be performed under local/regional anesthesia with or without maternal sedation. Maternal risks and risks to the mother's life are therefore minimal but not nil. We accept the risks involved after fully understanding them and agree to go ahead with the cystoscopic laser ablation of the PUV of our free will.

Patient's signature	Husband's/Relative's signature
Date/time	Date/time
Doctor's signature	

Pre-Op Checklist and Patient Preparation

- Serial vesicocentesis showing a favorable biochemical analyte profile is ideal but not mandatory.
- Preoperative hematological investigations including Rh typing.
- Preanesthetic checkup (PAC), particularly if epidural anesthesia is planned.
- Informed written consent.
- Intravenous (IV) cannulation.
- Test dose for sensitivity testing: antibiotic and lignocaine.
- Antibiotic prophylaxis: 1 g cefazolin/ceftriaxone 30 minutes before needle insertion/during surgical painting and draping (as per the institutional protocol of surgical prophylaxis).
- Injection of hydroxyprogesterone caproate 500 mg (Proluton Depot) intramuscular (IM) on the morning of the procedure.
- Nitroglycerin (NTG) patch 2 hours before the procedure.

Personnel Requirement

- Fetal interventionist.
- Pediatric urologist.
- Anesthesiologist (for epidural anesthesia or for intra-op emergency assistance).
- Assistant well versed in handling fetoscope, laser fiber, and ultrasound probe.
- Surgical assistant nurse.
- Sonography assistant to handle ultrasound machine.

Operating Room Requirements

The procedure may be performed in an operation theater or in an ultrasound room where the procedure can be performed under strict asepsis.

- A high-resolution ultrasound machine with color Doppler.
- Fetoscopy monitor.
- Standard surgical preparation set: sterile drapes, sponge forceps, and gauzes.
- Sterile probe cover, sterile jelly (Betadine solution can be used as an alternative).
- A no. 11 blade scalpel.
- One percent lignocaine 5 to 10 mL for local anesthesia.
- Fentanyl (2 µg/kg estimated fetal weight [EFW]) and pancuronium/vecuronium (0.1 mg/kg EFW) or atracurium (0.4 mg/kg EFW) for fetal anesthesia.
- Warm Ringer's lactate (RL) solution for continuous bladder irrigation
- Fetoscopy set with monitor: Introducer needle with a trocar, positioner, guidewire, and laser fiber.
- A 1.0-mm fetoscope (Karl Storz, Tuttlingen, Germany) with a 2.2-mm custom curved sheath (if a 1.3-mm fetoscope is used, the sheath used is 2.7 mm; similarly, if a 2.2-mm fetoscope is used, the sheath used is 3.3 mm)—the choice of the scope would be dictated predominantly by the gestational age.
- A 400-µm (before 20 weeks) or 600-µm (after 20 weeks) contact laser fiber.
- Nd:Yag (neodymium:yttrium aluminum garnet) laser machine (SmartEpil, DEKA, Florence, Italy).

- Alternatively, a diode laser (Dornier Medtech, Kennesaw, GA, United States) may be used.
- A 5-mL syringe (for lignocaine), a 1-mL syringe (for fetal anesthesia), and a 22-gauge spinal needle (for fetal anesthesia).

Procedure Steps

The procedure steps are the following (►**Video 1**):

1. Patient position: supine.
2. Perform ultrasonography on the table to confirm a favorable fetal position before painting and draping.
3. Once the fetal position is favorable, surgical paint and drape may be performed.
4. The assistant sanitizes the ultrasound probe with an antiseptic solution and a sterile probe cover is applied.
5. Repeat the ultrasonography and reconfirm a favorable fetal position to plan a route of entry.
6. Once the intervention is "good to go ahead" an IV fluid (at 80–100 mL/h) and oxygen through a face mask for the mother may be started.
7. Fetal anesthesia is given by combining fentanyl (2 µg/kg) and pancuronium (0.1 mg/kg; alternative: atracurium 0.4 mg/kg EFW), which are mixed in the same syringe and injected into the fetal thigh (or into fetal deltoid, according to ease of access) using a 22-gauge spinal needle.
8. Plan a route of entry and infiltrate lignocaine on the mother's skin and subcutaneous tissue up to the uterine serosa (try not to touch the serosa with the needle or move beyond to avoid inadvertent uterine contraction that might hinder the entire plan of entry).
9. A small cutaneous incision (stab incision) is to be made after confirming an adequate entrance point to the uterine wall, avoiding high-caliber vessels.
   After careful ultrasound examination of the position of the fetus and the placenta, the curved fetoscope is to be inserted percutaneously into the fetal bladder avoiding the placenta (direct insertion technique). Unlike in fetoscopy for twin–twin transfusion syndrome (TTTS), the Seldinger technique of entry is not preferred and often not possible (►**Video 1**).
10. While planning the route of entry into the fetal bladder, two important aspects are to be kept in mind is: (a) the route of entry should avoid fetal bowel and other viscera and (b) the entry point is through the upper part (dome) of the distended bladder.
11. The fetoscope is advanced into the fetal bladder and posterior urethra, carefully negotiating the bladder neck angle. (This is often difficult or not possible beyond 25–26 weeks of gestation.)
12. Continuous bladder irrigation is maintained with warm RL or saline.
13. The initial step is diagnostic: the bladder is examined thoroughly to confirm that the etiology of LUTO is PUV

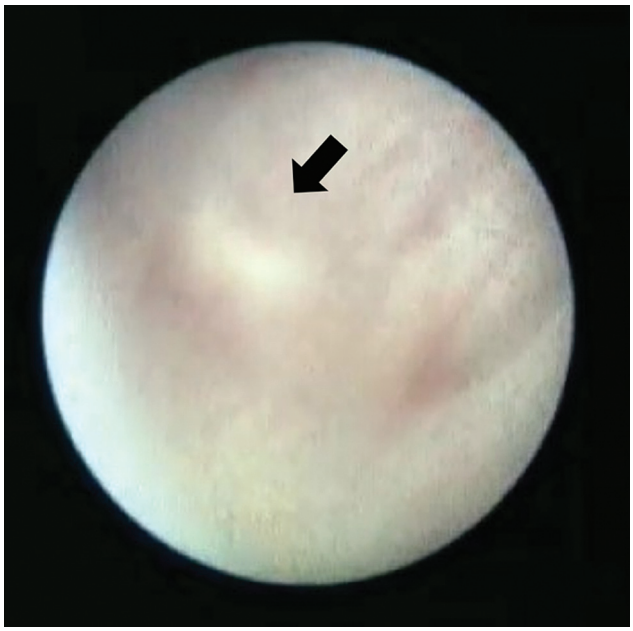

Fig. 2 Diagnostic fetal cystoscopic appearance of the posterior urethral valve, appearing as a glistening white membrane, occluding the urethral passage.

14. The diagnosis of PUV is confirmed if a white, membrane-like obstruction of the urethra is seen (►**Fig. 2**).
15. The identification of the verumontanum serves as a landmark to identify the valves.
16. If the diagnosis of PUV cannot be confirmed, the procedure should be abandoned at this stage.
17. Once PUV is confirmed, a 400-µm laser fiber is passed through the fetoscope.
18. Valve fulguration is accomplished by pulsed laser bursts using the lowest power setting (maximal setting of 30 W and 100 J with an Nd:YAG laser).
19. In the case of the diode laser, the settings used are 30 to 40 W and 800 to 1,000 J, continuous fire of 2 seconds, using a 600-µm contact laser fiber.
20. Postablation, urethral patency is confirmed when the bladder is found to be emptying and by visualizing a urinary stream through the urethra on Doppler ultrasonography and the appearance of amniotic fluid in the background of prior anhydramnios.
21. Small amounts of iatrogenic fetal ascites may be anticipated at this stage owing to urine leak from the fetoscope entry site and should not be a cause for concern.
22. Laser fiber and the fetoscope are withdrawn.
23. Fetal cardiac activity is documented at this stage.
24. An ultrasound scan is then performed to confirm bladder emptying and to rule out complications like a rectus sheath hematoma or free fluid in the flanks (indicative of leakage of amniotic fluid).
25. The incision site is closed with a Band-Aid or Steri-Strip.
26. The mother is shifted to the ward.

Video 1

Fetal cystoscopy. Online content including video sequences viewable at: https://www.thieme-connect.com/products/ejournals/html/10.1055/s-0044-1782222.

Post-Op Checklist

- Document the absence of free fluid in maternal flanks by ultrasound immediately postprocedure and after 3 hours.
- Document fetal heart activity at the end of the procedure and after 3 hours.
- A detailed procedure report is generated, and one copy is handed over to the mother at the time of discharge.
- The NTG patch may be applied for 24 hours: the patient should be warned of the possibility of severe headache owing to the vasodilatory effect of NTG and should be allowed oral/IV paracetamol for pain relief if required.

Postmonitoring of the Mother and the Fetus

- The mother is to be observed in the ward for a minimum of 3 to 4 hours post-op.
- She may be allowed to ambulate after around 30 minutes.
- Maternal blood pressure, pulse rate, and vitals should be monitored every 30 minutes for 2 hours and then every six hours for 24 hours.
- Fetal heart activity is documented during and at the end of the procedure and 24 hours post-op.
- Tocolysis: The NTG patch is discontinued after 24 hours. Indomethacin 25 mg every six hours (until 48 hours postprocedure)/alternatively tab nifedipine 10 mg twice a day $\times$ 3 days.
- The patient/prospective mother is allowed oral liquids as per demand. If an epidural had been administered, initially soft food is allowed; if it is well tolerated, then normal diet may be resumed after 3 to 4 hours.
- Analgesics may be prescribed if indicated.
- A scan is planned after 24 hours to document fetal cardiac activity and increase amniotic fluid volume with bladder emptying.
- The mother may be discharged from the hospital after 24 hours if there are no complications with the advice to avoid heavy physical exertion for a week.
- The mother is instructed to report to the hospital immediately if there is substantial leaking, bleeding, pain, or fever.
- Follow-up scans are scheduled after 1, 2, and 4 weeks from the procedure and thereafter as indicated.

Report Template

Patient's name:
Age:
Husband's name:
Hospital ID:
Gestational age:
Indication:
Procedure name:
Maternal anesthesia:
Fetal anesthesia:
Start time:
End time:
Control: continuous ultrasound guidance
Insertion needle: 22 gauge/2 mm
Laser used: Nd:Yag/diode (power)
Uterine entry: midline, right/left, upper/lower quadrant
No. of attempts: single/double/multiple
Fetal entry: left lateral abdomen/right lateral abdomen
Intraoperative complications:
Post-op advice:

Funding
None.

Conflict of Interest
None declared.

Suggested Reading

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