Year : 2016

Fetal laser therapy: applications in the management of fetal pathologies

MATHIS Jérôme

UNIVERSITE DE LAUSANNE - FACULTE DE BIOLOGIE ET DE MEDECINE

Département de gynécologie, obstétrique et génétique
Service d'obstétrique

Fetal laser therapy: applications in the management of fetal pathologies

THESE

préparée sous la direction du Docteur David BAUD

et présentée à la Faculté de biologie et de médecine de
l'Université de Lausanne pour l'obtention du grade de

DOCTEUR EN MEDECINE

par

Jérôme MATHIS

Médecin diplômé de la Confédération Suisse
Originaire de Wolfenschiessen (Nidwald)

Lausanne

2016

UNIL | Université de Lausanne
Faculté de biologie
et de médecine

Ecole Doctorale
Doctorat en médecine

Imprimatur

Vu le rapport présenté par le jury d'examen, composé de

Directeur de thèse	*Monsieur le Docteur* ***David Baud***
Co-Directeur de thèse	
Expert	*Monsieur le Professeur* ***Gerhard Gmel***
Directeur de l'Ecole doctorale	*Monsieur le Professeur* ***Niko Geldner***

la Commission MD de l'Ecole doctorale autorise l'impression de la thèse de

Monsieur Jérôme Mathis

intitulée

Fetal laser therapy: applications in the management of fetal pathologies

Lausanne, le 19 avril 2016

pour Le Doyen
de la Faculté de Biologie et de Médecine

Monsieur le Professeur John Prior
Vice-Directeur de l'Ecole doctorale

Résumé

Thérapie fœtale au laser: nouvelles applications dans la prise en charge des pathologies fœtales

Le traitement au laser par fœtoscopie est utilisé pour la coagulation d'anastomoses artério-veineuses dans le cadre de syndrome transfuseur-transfusé. Actuellement, certaines malformations peuvent être une indication à ce traitement comme le syndrome des bandes amniotiques, le choriangiome, l'obstruction de l'urètre, le kyste sacro-coccygien et les masses pulmonaires. Ces pathologies peuvent être létales sans intervention et ce traitement, encore expérimental, pourrait être proposé dans ces cas.

Il s'agit d'une méta-analyse et revue systématique de la littérature à l'aide de « PubMed », « Medline » et « Web of Science » dans laquelle nous avons recensé tous les cas publiés de traitement par laser durant la période fœtale depuis 1980. Cinq groupes de pathologie peuvent bénéficier de ce traitement et sont décrits séparément.

Le syndrome des bandes amniotiques peut engendrer une amputation du membre atteint par compression induisant une ischémie ou un décès fœtal si cette bande atteint le cordon ombilical.
De larges choriangiomes, tératomes sacrococcygiens ou masses pulmonaires peuvent mener à un hydrops fœtal par compression ou « vol vasculaire » menant dans les cas les plus sévères à la perte fœtale.
Des valves de l'urètre postérieur créent une obstruction induisant une mégavessie avec des répercussions rénales ainsi qu'une hypoplasie pulmonaire.

Le pronostic de ces différentes pathologies peut être fatal et les options thérapeutiques sont limitées. Dans certains cas, la thérapie au laser par foetoscopie peut changer ce pronostic.

Encore expérimentale, cette technique montre des résultats prometteurs. Le taux de réussite et le taux de survie dans les différentes catégories est encore perfectible. L'amélioration devra se faire aussi bien au niveau de l'indication opératoire et de la sélection des cas, de la technique et du matériel que de l'expérience des opérateurs. Cette technique peut offrir un espoir de survie pour des fœtus très certainement condamnés. Cette étude est basée essentiellement sur des petites séries de cas ou de cas unique, les résultats doivent donc être analysés avec prudence car des biais de report ou au niveau des investigateurs ne peuvent pas être exclus.

La prise en charge de tels cas doit se faire dans un centre de référence, la décision d'intervenir devrait être multidisciplinaire et les parents bien informés du pronostic.

REVIEW

Fetal laser therapy: applications in the management of fetal pathologies

Jérôme Mathis, Luigi Raio and David Baud*

Swiss Fetal Laser Group, University Hospital of Bern, University Hospital of Lausanne CHUV, Lausanne, Switzerland
*Correspondence to: David Baud. E-mail: david.baud@chuv.ch

ABSTRACT

Fetoscopic coagulation of placental anastomoses is the treatment of choice for severe twin-to-twin transfusion syndrome. In the present day, fetal laser therapy is also used to treat amniotic bands, chorioangiomas, sacrococcygeal teratomas, lower urinary tract obstructions and chest masses, all of which will be reviewed in this article. Amniotic band syndrome can cause limb amputation by impairing downstream blood flow. Large chorioangiomas (>4 cm), sacrococcygeal teratomas or fetal hyperechoic lung lesions can lead to fetal compromise and hydrops by vascular steal phenomenon or compression. Renal damage, bladder dysfunction and lastly death because of pulmonary hypolasia may be the result of megacystis caused by a posterior urethral valve. The prognosis of these pathologies can be dismal, and therapy options are limited, which has brought fetal laser therapy to the forefront. Management options discussed here are laser release of amniotic bands, laser coagulation of the placental or fetal tumor feeding vessels and laser therapy by fetal cystoscopy. This review, largely based on case reports, does not intend to provide a level of evidence supporting laser therapy over other treatment options. Centralized evaluation by specialists using strict selection criteria and long-term follow-up of these rare cases are now needed to prove the value of endoscopic or ultrasound-guided laser therapy. © 2015 John Wiley & Sons, Ltd.

Funding sources: David Baud is supported by the 'Fondation Leenaards' through the 'Bourse pour la relève académique', the Divesa Foundation and the Swiss National Science Foundation (SNSF no. 310030-156169).
Conflicts of interest: None declared

INTRODUCTION

Prenatal ultrasound studies now enable the early detection of fetal anomalies. Because prognosis may be poor in some severe malformations complicated by hydrops or alteration of fetal blood supply, fetoscopic laser therapies have been described as a treatment option. Fetal laser therapy was first used in complicated monochorionic pregnancies,[1–3] such as twin-to-twin transfusion syndrome (TTTS) or twin reversed arterial perfusion (TRAP) sequence. In this article, we review other potential indications for fetal laser therapy, such as amniotic band syndrome (ABS), chorioangiomas, lower urinary tract obstructions (LUTOs), sacrococcygeal teratomas (SCTs) and chest masses. Fetoscopic laser therapy for selective termination in monochorionic pregnancies[4–6] and TRAP[7–10] sequence have recently been reviewed and will not be discussed here.

METHODS

We performed a systematic literature search to find all articles included in this review. Relevant articles were identified using electronic databases (PubMed, Medline and Web of Science). Searches were limited to articles written in the English language from 1980 to October 2014. All primary articles and reviews were examined to search for additional references. After reviewing all articles, cases reported only as an abstract were excluded. The following terms representing fetal conditions were used ('identification' part): 'amniotic band', 'chorioangiomas' and 'SCTs'. When reviewing the urinary tract chapter, the terms 'low urinary tract obstruction', 'urethral valves', 'megacystis' and 'ureterocele' were used. When reviewing the fetal lung mass chapter, the terms 'congenital cystic adenomatoid malformation', 'bronchopulmonary sequestration', 'lung mass' and 'lung tumor' were used. The following terms were added for possible treatment described in this review ('screening' part): 'fetal laser', 'fetal therapy', '*in utero* treatment' and 'prenatal intervention'. Flowcharts for each condition are available as supplementary figures.

Studies exploring the combination of a medical condition and its treatment were considered suitable for inclusion. Two authors (JM and DB) reviewed all abstracts independently. Agreement about potential relevance was reached by consensus with LR, and full text copies of those articles were obtained. Two reviewers (JM and DB) extracted relevant data regarding study characteristics and pregnancy outcomes. Inconsistencies were discussed by all authors, and consensus was reached. The assessment of the potential publication bias was problematic because of scarce number of studies and sparse events.

RESULTS

Incidence, pathophysiology, prenatal and postnatal natural history of fetal conditions as well as the aims, indications and alternatives to fetal laser therapy have been summarized in Table 1.

Amniotic band syndrome

Distal edema and venous or arterial blood flow obstruction are best evaluated by ultrasound and Doppler studies. Weekly monitoring by Doppler studies had been proposed by Richter *et al.*, allowing a comparison of the affected limb with the controlateral side as a control.[11,12] Although cases of spontaneous resolution have been described,[11,13–15] early prenatal diagnosis of severe cases may benefit from *in utero* lysis of the bands, restoring blood flow to the affected limb (Figure 1).

Initial studies performed on lambs demonstrated that early release of amniotic bands allowed for recovery of the limb's structure and function after fetoscopic laser therapy.[16,17] In 1997, Quintero *et al.* successfully attempted the first human amniotic band release using laser therapy [yttrium aluminum garnet (YAG)] under fetoscopic and ultrasound guidance at 23 weeks of gestation. Intraoperative bleeding complicated the fetoscopic approach, resulting in an incomplete release of the limb, but functionality was successfully restored[18] (Table 1). Peiro *et al.* reported a case of fetal therapy of ABS of the umbilical cord,[19] diagnosed during a limb amniotic band fetoscopic procedure at 21 weeks. Z-plasty was performed in the postnatal period, and thus, full function of the limb was present at 9 months.[19]

To date, 19 *in utero* treatments of ABS have been reported in the literature[10,12,15,17–27] (Table 2), 13 using laser therapy,[12,17–23] 4 using scissors[15,18,24] and 2 via blunt dissection.[25] All laser procedures were performed between 19 and 23 weeks using YAG laser (except 1 case with a diode laser at 25-watt power[12]). Unfortunately, the energy required to section the amniotic band was never described. A unique uterine entry was feasible in 8 cases, whereas 3 cases required two ports: 1 case was assisted by maternal laparoscopy and the other case by maternal laparotomy. Partial laser section of the ABS was feasible in all cases; however, complete release was only achieved in 6 cases.[17–19]

All but 4[12,26,27] laser procedures (69%) were complicated by premature preterm rupture of membrane (PPROM). PPROM occurred within 24-hour post-procedure for 2 cases,[17,19] and within a mean of 5 weeks following the other cases (ranging 0.4–9 weeks). All women delivered preterm between 6 and 13 weeks post-laser procedure (mean 10 weeks).

After laser treatment, seven of 11 cases (64%) had fully functional limbs,[12,17–20,26,27] 1 case had limited range of motion[20] and 3 cases resulted in a limb amputation despite *in utero* treatment.[20] In ABS treated with other *in utero* approaches, amniotic bands were sectioned with scissors in 3 cases. One case was complicated by radial paresis of the left arm[18], whereas another had a fully functional limb.[24] The last case resulted in a fully functional leg despite failure of the surgical procedure.[15]

Limbs that have undergone fetoscopic release appear grossly normal even though histological changes can persist, including venous and lymphatic congestion.[16] After birth, most cases required Z-plasty to restore the aesthetic aspect with acceptable results.[12,17–19,26,27]

Pseudo-ABS is an iatrogenic complication following an invasive procedure, namely amniocentesis, amnioreduction, fetoscopy or septostomy in twins.[28,29] To our knowledge, fetoscopic release of pseudo-ABS has never been described.

Fetoscopic laser treatment may be considered when blood flow is impaired although still present.[12] Patients, however, should be informed that (1) ABS is a non-lethal condition in most cases; (2) prenatal intervention carries significant fetal morbidity mainly linked to the consequences of PPROM and preterm birth, with possible mortality; (3) *in utero* treatment does not guarantee functionality and (4) absence of prenatal treatment might also result in full functionality. The risk/benefit balance between *in utero* and postnatal treatment should be discussed together with plastic and orthopedic surgeons.

Chorioangioma

Details regarding placental chorioangiomas[30–32] and treatments other than laser therapy[33–45] are described in Table 1.

Bhide *et al.* described the first case of interstitial laser therapy performed in a 23-week pregnant woman presenting with a large chorioangioma.[46] Quarello *et al.* described the first fetoscopic assisted laser coagulation of a chorioangioma.[47]

To date, 12 large chorioangiomas have been treated with laser therapy between 24 and 32 weeks of gestation (Table 3). Interstitial (4 cases[48–50]) or superficial (fetoscopic guided or ultrasound-guided[47,49–54]) laser techniques were used. A YAG laser was used in 6 cases, with a power range between 20 and 40 W. All cases but one[48] were complicated by polyhydramnios, and amniodrainage was performed in 6 of those cases. Two cases[48,50] required a second procedure within 10 days after the first fetoscopic laser therapy. Among the 12 fetuses with large chorioangiomas treated with fetoscopic laser therapy, 9 (75%) fetuses were live born (including one monochorionic twin pregnancy with fetal demise of one twin) of which one fetus died within a year after birth because of chronic renal insufficiency.[49]

Indication for prenatal intervention should only be discussed in cases with high-output failure (Table 1). The results of treating symptomatic giant chorioangiomas are similar for all approaches (arrest or reduction of blood supply). The choice of technique should be based on (1) the location of the placenta and the chorioangioma, (2) the accessibility of the tumor and feeding vessel by fetoscopy or by ultrasound guided techniques, (3) the diameter of this vessel and (4) the experience of the fetal therapy center. Definitive treatment can be achieved using endoscopic laser therapy by coagulation of the feeding vessel. This may be complicated by bleeding, exanguination or demise of the fetus. An uneventful perinatal outcome should be expected in cases of successful coagulation.

Lower urinary tract obstruction

Fetal interventions have been suggested for the treatment of severe congenital LUTO[55–58] but should only be discussed and offered to selected cases as described in Table 4.

The effectiveness of vesico-amniotic shunting (VAS) as a treatment for LUTO was tested in the percutaneous shunting in lower urinary tract obstruction (PLUTO) randomized control trial.[59] Because of poor recruitment, however, effectiveness remains uncertain. Among survivors, renal function remains

Table 1 **Description of the fetal conditions presented in this review**

	Incidence[a]	Pathophysiology	Prenatal natural history	Postnatal natural history	Aim of fetal laser therapy	Indication for fetal therapy	Alternatives to fetal laser therapy
Amniotic band syndrome	1/1200–1/15 000	• Early rupture of the membrane • Results in amniotic bands that insert on the body of the fetus or its ombilical cord	Constriction leading to venous obstruction, edema, complete vascular obstruction	• Lymphedema • Limb amputation • Limb deep scar • facial clefts • abdominal wall dysruptions • anencephaly	Release the band(s) before irreversible ischemia	• Evidence of compromised blood supply • Dopplers comparisons with the controlateral extremity or previous evaluations	• Fetoscopy and section of the band(s) with scissors[15,18,24,27] • Mechanical releasing[25,27]
Chorioangioma	1/100 But large tumors in 1–3/9000	• AV shunt • leads to vascular steal	If >4 cm, risk of: • abruptio placentae • non-immune hydrops • hydramnios and preterm delivery • fetal anemia and thrombocytopenia • high-output heart failure • maternal mirror syndrome	• Complications from prenatal state • Overall mortality 30% (half intrauterine)	Interruption of the vascular supply to the mass	• Fetal high-output heart failure prior to viability • Symptomatic hydramnios	• Intrauterine transfusion[33–35] • Amniodrainage[36] • Injection of absolute alcohol[30,31,37–39] • Injection of sclerosant agents[40–43] • Embolization[44] • Endoscopic-guided ligation of feeding vessel[48]
Lower urinary tract obstruction (LUTO)	1–2/3000	• Bladder outflow obstruction • Secondary to posterior or anterior urethral valves, urethral atresia or stenosis	• Megacystis • Progressive bilateral hydroureter and hydronephrosis • Renal damage • Anhydramnios • Associated structural and chromosomal disorders	• High perinatal mortality and morbidity because of pulmonary hypoplasia and severe renal impairment. • May necessitating dialysis and renal transplantation • Bladder dysfunction, incontinence and orthopedic problems	Fulguration of the (anterior or posterior) valves through fetal cystoscopy	• Extremely dilated bladder • Increased wall thickness • Dilated urethra ('keyhole sign') • Bilateral hydronephrosis • Oligohydramnios • 'Favorable' fetal urinalysis • Normal male karyotype • No additional fetal malformations	• Vesico-amniotic shunt[55,57,59]
Saccrococcygeal teratoma	1–4/40 000	• Benign sacral mass • Composed of cystic/solid/mixed tissues • AV shunt leading to vascular steal if solid large vascularized tumor	If large solid and vascularized mass, similar risks as chorioangioma	• Tumor dystocia at birth • Resection because the risk of malignancy increases with delayed excision • May cause bladder outlet obstruction, rectal atresia, sacral bone deformity	Superficial or intratumoral reduction/interruption of the vascular supply to the mass	Fetal high-output cardiac failure prior to viability	• Open fetal surgery,[78,88–90] • Thermocoagulation[91] • RFA[92] • Histoacryl embolization[80,93] • Coiling[84] • Alcohol sclerosis[94]
Fetal hyperechoic lung lesions	1/15 000	• Impair lung development • Broncho-pulmonary sequestration (BPS) • Congenital pulmonary airway malformation (CPAM)	If large tumor and venous return compression, risks of non-immune hydrops, polyhydramnios, heart failure, growth restriction, fetal demise	• Pulmonary hypoplasia • Perinatal death	Interruption of the vascular supply to the mass	Fetal hydrops prior viability	• Steroids[108,109] • Open fetal surgery[90,100] • Thoracoamniotic shunting[110] • Occlusion of vascular supply[107,113] • Injection of sclerosing agent[112–114] • Coiling[107] • RFA[107]

RFA, radio frequency ablation; AV, arterio-venous.
[a](1/pregnancy).

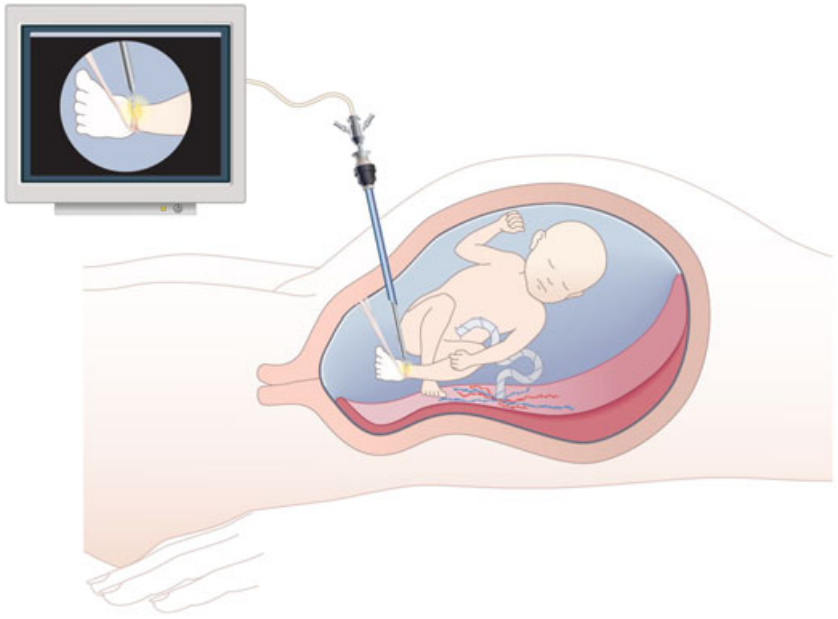


Figure 1 (Amniotic band syndrome): Picture illustrating placement of the laser fiber for the fetal treatment of an amniotic band syndrome

poor irrespective of whether VAS was performed or not,[59] as suggested in previous studies.[60] A recently published retrospective single center study, however, demonstrated that VAS may still be a valid treatment option in adequately selected cases.[55] Complications of VAS include shunt blockage, migration, dislocation and iatrogenic gastroschisis.[57,59]

The use of fetal cystoscopy in diagnosis and treatment of posterior urethral valves (PUV) has recently been proposed.[56,61–63] This procedure may have significant advantages over VAS because it (1) allows visualization of the posterior urethra and may differentiate between PUV and urethral atresia, (2) avoids frequent re-interventions that are often necessary because of shunt dislocations, (3) may have the potential to allow a more physiological release of the obstruction and drainage and (4) negates the need of amnioinfusion prior to the procedure.[56,63]

Fetal cystoscopy therapy has shown promising results for the treatment of PUV.[10,56,61,64–67] To date, 52 reported fetal cystoscopies have been performed,[56,61–66,68–74] 26 of them using cystoscopic laser fulguration[61,66,67,73] and 9 using other methods (reviewed in Ruano,[56] specifically 1 monopolar fulguration,[71] 1 urethral probing,[72] 4 guide wires and 4 hydroablations[64]). Sananes *et al.* recently reviewed the technical aspects and complications of PUV cystoscopic laser fulguration from three different fetal centers.[61] The procedure seems to be optimal (Figure 2) (1) under maternal epidural or local anaesthesia, (2) with fetal immobilization and anaesthesia, (3) using a 1.0-mm fetoscope with a 2.2-mm custom curved sheath and (4) with a 400-μm (before 20 weeks) or 600-μm (after 20 weeks) contact laser fiber. The diagnosis of PUV is confirmed if a membrane-like obstruction of the urethra is seen through which saline can be injected.[56,65] The PUV can be fulgurated by pulsed laser bursts using the lowest power setting (maximal setting of 30 W and 100 J with a YAG laser).[61] Urethral patency is confirmed when the bladder is found to be empty and by visualizing a urinary stream through the urethra on Doppler ultrasonography.

Formation of a urological fistula appeared to be the main adverse complication following cystoscopic laser fulguration of PUV. This complication was observed more frequently in cases with a higher gestational age at time of surgery, non-immobilized fetuses, absence of 'keyhole' sign and use of semi-curved instruments, the Diode laser or elevated laser power and energy settings.[61] The authors highlight that cystoscopic laser fulguration of PUV is technically more complex than VAS, requiring specific fetoscopic instruments, skills and the assistance of a pediatric urologist.[61]

When considering all 26 cases treated by fetal cystoscopic laser fulguration,[61,66,67] a total of 16 infants survived (62%), among them, 14 (88%) had a normal renal function. In comparison, the PLUTO trial reported only 2/12 (17%) and 0/12 (0%) live births with normal renal function at 2 years of life after VAS and conservative management respectively.[59] Despite poor data exist on 2 years or long-term follow-up after cystoscopic laser fulguration of PUV, further studies are needed to demonstrate the benefit of this treatment option.

Two additional causes of megacystis have literature documenting treatment with laser fulguration, that is, anterior urethral valves[75] and ureterocele.[76] Sago *et al.* performed a fetal urethrotomy by laser for anterior urethral valves diagnosed at 17 weeks of gestation (YAG laser under a 1-mm fetoscope).[75] Despite technical success, chorioamnionitis and subsequent intrauterine fetal death were observed on day 3. Soothill et *al.* successfully treated a 28-week female fetus suffering from a ureterocele associated with bilateral hydronephrosis and distended bladder (using a 400-μ laser fiber through a 19 gauge needle under ultrasound guidance).[76] After delivery at 38 weeks, the kidneys showed minor dilation and the renal function was normal.

In conclusion, 'urologic' fetal laser therapy is feasible and can be used for treatment of megacystis because of posterior

Table 2 **Amniotic band syndrome: Outcomes of fetuses treated *in utero* for amniotic band syndrome**

	Intervention										
References	Endoscope	Angle	Trocar	Nb. ports	Type	GA at procedure (weeks)	Affected limb	Complete release of the amniotic band	PPROM (weeks)	Delivery (weeks)	Outcome
Laser											
Quintero *et al.* (1997)[18]	2.7 mm	0°	NA	2	400 µm-YAG	23	Left ankle	No	31	34.5	Full functionality
Keswani *et al.* (2003)[20]	NA	NA	4 mm	1	600 µm-YAG	23	Left wrist	No	27	33	Limited range of motion
Keswani *et al.* (2003)[20]	NA	NA	4 mm	1	400 µm-YAG	19	Right wrist and hand	No	19.4	32	Final amputation of hand
Hüsler *et al.* (2009)[22]	1 mm	NA	2.2 mm	2	600 µm-Diode 30 W	22	Right forearm	No	—	—	Fetal demise after 3 days
Soldado *et al.* (2009)[23]	2 mm	0°	3 mm	1	YAG	22	Left leg, right thigh	Yes	31	31	Full functionality
Soldado *et al.* (2009)[23]	2 mm	0°	3 mm	1	YAG	22	Left leg, left hand syndactyly	Yes	22	28	Full-functionality
Peiro *et al.* (2009)[19]	2 mm	0°	10 Fr	1	YAG	22	Left leg and umbilical cord	Yes	22	28	Full functionality
Richter *et al.* (2012)[12]	2.9 mm	30°	10 Fr	1	600 µm-Diode 25 W	23	Right forearm	No	—	36.3	Full functionality
Javadian *et al.* (2013)[26]	2 mm	0°	NA	1[a]	600 µm-Diode 25 W and microscissors	22	Right hand	Yes	—	37.6	Amputation to tip of a finger and two toes
Javadian *et al.* (2013)[26]	2 mm	0°	NA	1	600 µm-Diode 25 W	21	Both hands and umbilical cord	No	33.5	33.6	Amputation of digits[b]
Derderian *et al.* (2014)[27]	NA	NA	3 mm	1	YAG	19	Both legs and umbilical cord	NA	—	—	IUFD
Derderian *et al.* (2014)[27]	NA	NA	3 mm	1[f]	YAG	24	Left arm and umbilical cord	Yes	—	40	Full-functionality
Derderian *et al.* (2014)[27]	NA	NA	3 mm	2	YAG	22	Right arm and umbilical cord	Yes	—	40	Full-functionality
Scissors											
Quintero *et al.* (1997)[18]	2.7 mm	5°	[d]	2	—	22	Left arm	Yes	—	39	Radial paresis left arm
Sentilhes *et al.* (2004)[15 c]	3 mm	0°	4 mm	1	—	28	Right lower leg	No	32	33	Full-functionality
Ronderos-Dumit *et al.*(2006)[24]	2.7 mm	5°	[e]	2	—	23	Right lower leg	No	37.3	37.4	Full-functionality
Derderian *et al.* (2014)[27 g]	NA	NA	3 mm	2[f]	+hook cautery	24	Left leg and umbilical cord	Yes	32.4	32.4	Full-functionality
Mechanical lysis											
Assaf *et al.*(2012)[25]	NA	NA	NA	1	—	29	Right lower leg	Yes	—	38	Amputation right sec. toe
Derderian *et al.* (2014)[27]	NA	NA	3 mm	1[f]	—	24	Right arm	No	—	32	Full-functionality

NA, not available; IUFD, in utero fetal demise; GA, gestational age; PPROM, preterm premature rupture of membranes.
[a]Laparoscopy-assisted fetoscopy with two abdominal trocars (anterior placenta).
[b]Defect already observed during the fetoscopy.
[c]Unsuccessful therapy because of *in utero* bleeding and malposition of the fetus.
[d]Bleeding at the level of the second trocar, which was thus not used.
[e]Size of first trocar not mentioned; second trocar 2.5 mm.
[f]Maternal laparotomy.
[g]Twin-to-twin transfusion syndrome at 17 weeks treated with radio frequency ablation of one fetus. ABS in fetus who survived.

Table 3 Chorioangioma: Outcomes of fetuses treated *in utero* for chorioangioma by laser photocoagulation, alcohol injection, sclerosant agent injection, embolization or endoscopic ligation of the feeding vessel

References	Size of choriangioma (mm)	GA at procedure (weeks)	Fetoscope (mm)	Therapeutic approaches	Type of ablation	Blood flow after procedure	Associated amnio-drainage	Associated blood transfusion	GA at delivery (weeks)	Outcome
Laser										
Bhide *et al.* (2003)[48]	53 × 45 × 44	25 + 4		ND : YAG; 400 um, 20 W	Interstitial	No	No	No	32 + 3	Alive
Quarello *et al.*(2005)[47]	38 × 34 × 44	25	2	diode laser; 400 um, 30 W	Vascular	No	1500 mL	No	39	Alive
Bermudez *et al.* (2007)[51]	53 × 48 × 61	24		ND : YAG; 40 W	Vascular	No	2800 mL	Yes		Fetal demise
Sepulveda *et al.* (2009)[49]		26	2.5	optical fiber; 600 um, 30–40 W	Vascular	No	2300 mL	No	37	Alive
		27	2.5	optical fiber; 600 um, 30–40 W	Vascular	Yes	Yes	Yes	28	Death one year after birth
		28	2.5	optical fiber; 600 um, 30–40 W	Interstitial	NA	No	No		Fetal demise
Mendez-Figueroa *et al.* (2009)[52]	80 × 75 × 80		2	diode laser; 600 um, 25-35 W	Vascular	No	1800 mL	Yes		Fetal demise
Zanardini *et al.* (2010)[50 b]	42	24 + 3		ND : YAG - 400 um, 20 W	Vascular	NA	No	No	36 + 3[c]	Fetal demise[c]
	35	32 + 3		ND : YAG; 400 um, 20 W	Interstitial	NA	No	No	39 + 1	Alive
	54	29 + 2		ND : YAG; 400 um, 20 W	Interstitial	NA	No	Yes	37 + 3	Alive
Jones *et al.* (2012)[53]	71	27 + 4	3.3	ND : YAG; 600 um, 30 W	Vascular	No	1010 mL[d]	No	38 + 6	Alive
Jhun *et al.* (2014)[54]	156 × 112 × 106	29 + 1			Vascular	Yes	645 mL	No	33 + 4	Alive
Alcohol injection										
Nicolini *et al.* (1999)[37]	60 × 35 × 30	27		absolute alcohol	Vascular	No	1700 mL	No	Term	Alive
	50	24 and 25		absolute alcohol	Vascular	Yes	No	No	Term	Alive
Jauniaux and Ogle (2000)[31]	100	32		absolute alcohol	Vascular	No	No	No	32	Early neonatal death
Wanapirak *et al.* (2002)[38]	80	27		absolute alcohol	Vascular	No	Yes	No	32	Alive
Sepulveda *et al.* (2003)[30]	75	26		absolute alcohol	Center tumor	Yes[e]	No	No		Fetal demise
Deren *et al.* (2007)[39]	83 × 72	25 and 26		absolute alcohol	Center tumor	Yes	No	Yes	28	Alive
Sclerosant agents injection										
Lau *et al.* (2005)[41]	90	24		Enbucrilate	Vascular	No	No	No	26	

Gajewska *et al.* (2010)[43]	80 × 70 × 70	23 and 23 + 4	Glubran	Vascular	No	No	No	38	Alive
Babic *et al.* (2012)[40]	58 × 56 × 42	22	Enbucrilate	Vascular	No	3000 mL	Yes	30 + 3	Alive
Bolla *et al.* (2014)[42]	62 × 44 × 56	22	Cyanoacrylate	Vascular	No	No	No	37 + 2	Alive
Embolization									
Lau *et al.* (2003)[44]	100	24 and 25	Microcoil	Vascular	Yes	No	Yes (4)	29	Early neonatal death
Endoscopic-guided ligation of feeding vessel, bipolar electrocautery of superficial vessels									
Quintero *et al.* (1996)[45]	85	24	5[a]	Vicryl 3.0 + bipolar electrosurgery	Vascular	No	No	No	NA	Death after 3 days

NC, not confirmed, parents declined autopsy; NA, not available; ND, YAG: neomymium-doped yttrium aluminum garnet; GA, gestational age.
[a]Performed using two trocars.
[b]Four cases are reported in this study, but one already described by Bhide *et al.* (2003).
[c]Monochorionic twin pregnancy, fetal demise of recipient twin and survival of donor twin.
[d]Amniodrainage performed 1 week before laser.
[e]Transfer of alcohol in the fetal circulation and acute thrombosis of the umbilical vein leading to bradycardia and fetal death.

or anterior urethral valves or a large ureterocele. Despite promising early results, however, further experience will be required to evaluate the therapeutic value of this procedure in the management of LUTO. Intraoperatively, if cystoscopy fails to show the presence of a urethral valve, VAS can still be performed through the same trocar. Considering the lack of results in the PLUTO trial,[59] a randomized control trial comparing the various available therapies should be conducted. The PLUTO trial was not completed essentially because of recruitment challenges for the placebo arm. Comparing two therapies (VAS vs fetal cystoscopic laser therapy) may improve recruitment.

Sacrococcygeal teratoma

Most SCTs are benign, slow-growing tumors and resectable after birth.[77,78] A minority of SCTs are fast-growing, solid and highly vascularized teratomas, which can lead to several complications such as tumor rupture, hemorrhage, high cardiac output failure, hydrops and even fetal demise.[78,79] Mortality rates have been described as high as 25 to 37%[80] but can be much higher when hydrops occurs.[77]

Once the fetus is viable, premature delivery and postnatal surgery are preferred to avoid intra-uterine death in cases of fetal decompensation, thus allowing a survival rate of nearly 50%.[81,82] Prior to fetal viability, the management of hydropic SCTs is more challenging and controversial.[83,84] Without any treatment, intrauterine fetal demise occurs almost invariably[84,85] and mirror syndrome might compromise maternal health.[86,87]

Open fetal ablative surgeries have been attempted to prevent fetal demise,[78,88–90] thus improving fetal survival rate.[88] Surgery, however, is associated with major fetal and maternal risks such as preterm rupture of membranes, preterm delivery, uterine scarring, hemorrhage or infection.[88] In order to reduce these complications, devascularization of the tumor using minimally invasive procedures such as thermocoagulation,[91] radiofrequency ablation,[92] histoacryl embolization,[80,93] coiling[84] and alcohol sclerosis[94] has been described by several authors. Van Mieghem *et al.* systematically reviewed the literature regarding these therapeutic options for fetuses suffering from SCTs and presenting cardiovascular compromise prior to fetal viability.[84] Thirty-four SCT cases undergoing minimally invasive procedures have been identified. These invasive procedures intend to interrupt blood flow and arrest tumor growth, thus reversing cardiac failure and preventing further development of fetal anemia.[84] Among them, 10 cases were performed with laser energy[84,94–97] (Figure 3).

Hecher *et al.* reported the first SCT treatment using fetoscopic laser coagulation.[95] In contrast to this, first case where superficial fetoscopic laser coagulation was used in a non-hydropic fetus,[95] all 9 other SCT cases were hydropic and 8 were treated using interstitial laser.[84,94,96,97] Two of these eight cases were performed after unsuccessful coiling attempts.[84] PPROM occurred in at least 2 cases,[84,97] and all patients delivered before 32 weeks of gestation. Intra-uterine and neonatal deaths occurred respectively in 4 and 2 of the 10 SCT cases treated with laser coagulation, consequently leading to survival of 4 infants overall (40%).

Table 4 **Lower urinary tract obstruction: Outcomes of fetuses treated *in utero* for lower urinary tract obstruction by cystoscopic laser photocoagulation**

References	Number of cases treated with laser	GA at laser surgery (weeks)	Alive at birth	Normal renal function (in alive newborn)	Complications (in alive newborn)
Quintero *et al.* (2000)[66]	1	26	1/1	1/1	No
Holmes *et al.* (2001)[67]	2	22–25	1/2	1/1	No
Ruano *et al.* (2010)[73]	7	19–22	5/7	5/5	No
Ruano *et al.* (2011)[65]	3	16	2/3	2/2	No
Sananes *et al.* (2014)[61]	13[a]	18–26	7/13	5/7	One urological fistula

[a]Twenty three cases described in this study, but 10 cases already described in the two studies from Ruano.

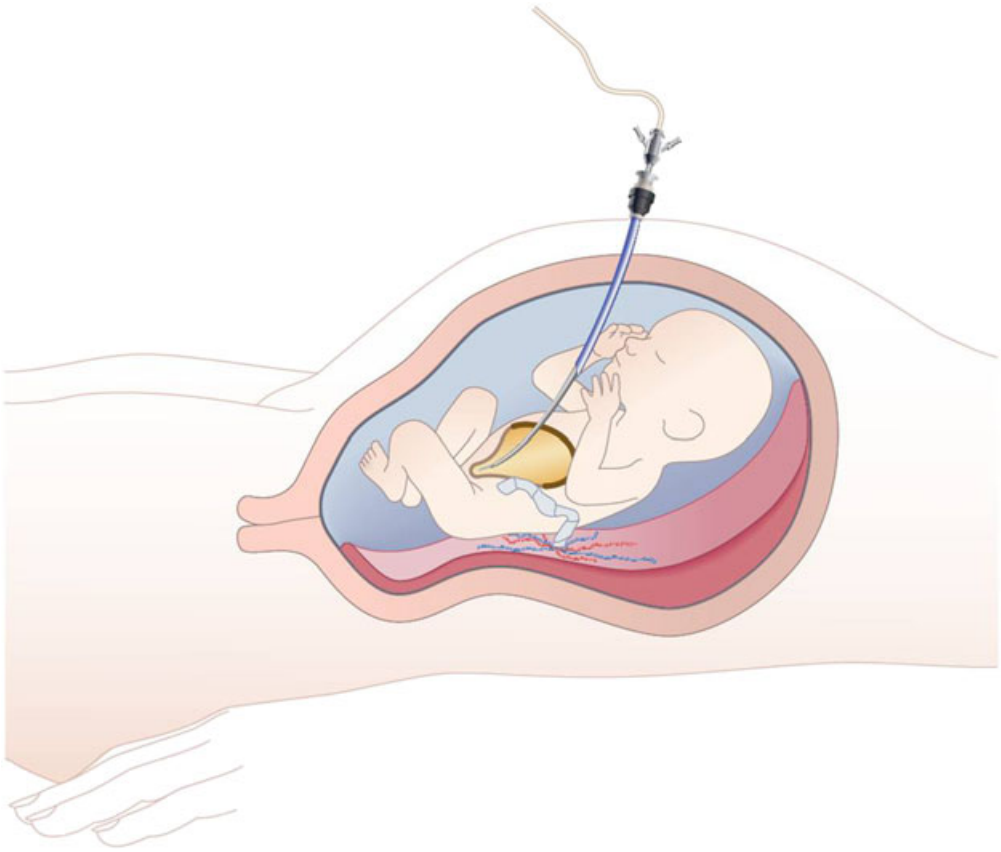


Figure 2 **(Megacystis): Picture illustrating placement of the laser fiber for the fetal treatment of posterior urethral valves (PUV)**

Both minimally invasive and open fetal surgeries remain controversial.[83,84] None of the interventions are free from procedure-related complications such as death, PPROM and preterm birth delivery.[77] The large amount of necrotic tissue left *in utero* after vascular ablation may be responsible for the high rate of preterm birth despite technical success.[90] Fetal therapy should only be discussed in cases with hydropic SCT before viability.

Further reports will be needed to address which therapeutic option improves fetal outcome.

Fetal hyperechoic lung lesions

The most common echogenic fetal lung malformations are broncho-pulmonary sequestration (BPS), congenital pulmonary airway malformation (CPAM) or 'hybrid' lesions that contain features of both BPS and CPAM, congenital high airway obstruction syndrome (CHAOS) and bronchial atresia (BA).[98–100] Note that CHAOS cases that are not eligible for *in utero* laser therapy should benefit from ex utero intrapartum treatment (EXIT) procedures.[101]

BPS is a non-functioning pulmonary mass vascularized by systemic circulation. In contrast, most cases of CPAM depend on the pulmonary blood supply. The differential diagnosis of these two benign lung masses is usually based on the identification of the feeding vessel using color Doppler ultrasonography.[98–100,102,103] The prognosis of these congenital lung lesions is usually good, except if complicated by hydrops fetalis with a mortality rate close to 100%.[99,100,104–107] Several prenatal interventions have been described (extensively reviewed in Witlox *et al.* and Khalek and Johnson [99,100]),

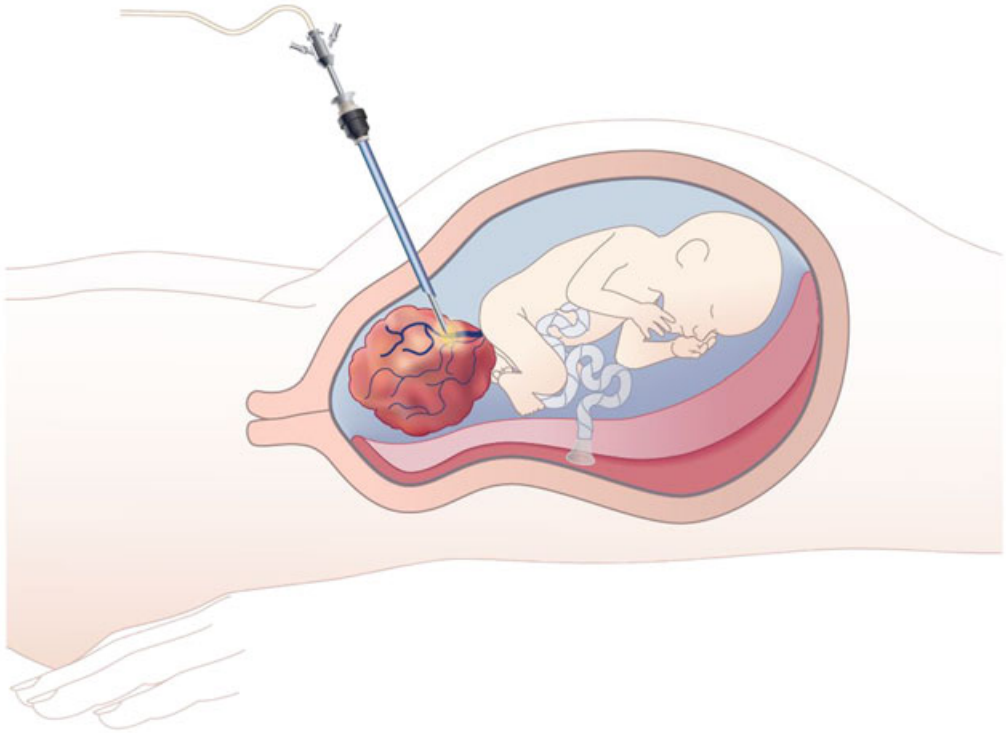


Figure 3 (Saccrococcygeal teratoma): Picture illustrating placement of the laser fiber for the fetal treatment of a saccrococcygeal teratoma

including steroids treatment,[108,109] open fetal surgery,[90,100] thoracoamniotic shunting for large cystic lesions[110] as well as occlusion of the vascular supply of the lung mass.[107,111] The latter can be achieved under ultrasound guidance either by injection of a sclerosing agent,[112–114] coiling,[107] radiofrequency ablation[107] or laser ablation[111] to treat massive CPAM.

Mixed results were obtained in cases with open fetal surgery as there was a high risk of premature labor as well as consequences for future pregnancies.[98] Regarding minimally invasive fetal interventions, ultrasound-guided laser therapy seems to be the most promising approach.[107,111]To To date, a total of 25 hydropic fetuses with lung masses have undergone percutaneous laser ablation (17 BPS and 8 CPAM),[98,104,107,111,115–121] (reviewed by Ruano *et al.*[111]). Fetal procedures were best performed under fetal anesthesia (fentanyl 15 μg/kg) and paralysis (pancuronium 2 mg/kg) by either umbilical vein or intramuscular injection. In all cases, a 400 or 600-μm laser fiber was passed through the lumen of an 18G-needle and the coagulation was performed with a Nd : YAG laser (15–50 W). In fetuses with BPS, a 'vascular ablation' was carried out with a laser fiber placed almost in contact with the abnormal 'feeding vessel' identified by color flow Doppler. The procedure is complete once blood flow through the feeding vessel has stopped.[107,111,118] In fetuses with micro-cystic CPAM, an interstitial ablation is performed after the insertion of the tip of the needle and the laser fiber into the fetal lung lesion. Both are then slowly withdrawn, while the tumor is being photocoagulated from the distal to the proximal border. Several passages may be necessary to obtain a reduction in vascular flow by Doppler analysis.[111,116,117] The procedure ends when a distinct 'echogenic area' is noted.

Overall (Table 5), median gestational age at the time of the laser procedure was 25 weeks (ranging 19–32). Thoracoamniotic shunting was used in 3 cases,[107,121] which may have had a beneficial adjuvant effect. Persistence or reoccurrence of tumor blood flow occurred in 13 (52%) cases[104,111,115,116,119,121], and a second intervention was needed in 7 (28%) cases an average of 5 weeks (ranging 1–12) after the first laser. There were 3 (12%) fetal deaths,[111,116] 4 (16%) neonatal deaths[98,104,111] and 18 (72%) live births. Survival rate was better for BPS (16/17, 94%) compared with CPAM (2/8, 25%, $p = 0.001$), which indicates that vascular laser ablation may be more effective than interstitial laser ablation.[111] Moreover, interstitial laser therapy may have increased potential for harm in fetuses with CPAM because collateral damage in a hydropic fetus is difficult to control. Placing a laser fiber into the hilar area of the lung and then slowly withdrawing it in a non-lobar, non-anatomic fashion might damage critical structures such as non-involved lobar vessels, bronchi or the phrenic nerve with significant secondary neonatal morbidity. This may suggest that other options, such as steroid treatment currently showing promise in the literature, should be considered in cases of hydropic CPAM.[109,122]

The mean gestational age at delivery was 37.1 weeks (ranging 29–41) for all live births after laser therapy for lung masses (including neonatal deaths). Postnatal surgery (lobectomy or sequestrectomy) was reported in 10 infants (10/17, 59%). No maternal complications have been reported in the literature.

Fetal bronchoscopy associated with laser therapy has recently been described for the treatment of CHAOS,[123] BA[124] and CPAM associated with BA.[125] In CHAOS,[123] one procedure was performed at 21.6 weeks of gestation under general maternofetal anaesthesia. Fetal laryngoscopy using a

Table 5 **Lung masses: Outcomes of fetuses treated *in utero* for lung masses by laser photocoagulation and bronchoscopy**

References	Number of patients	Postnatal diagnosis	GA at procedure (weeks)	Associated thoracic shunt	GA at second procedure	ND: YAG Power (Watt)	Total energy (J)	Local of ablation	Blood flow after procedure	Resolution of hydrops	GA at delivery (weeks)	Outcome	Postnatal surgery
Trans-thoracic													
Fortunato *et al.* (1997)[115]	1	CPAM	21	No	23	16	NA	Interstitial	Yes	Yes	NA	Alive	NA
Bruner *et al.* (2000)[116]	1	CPAM	22	No	24	15	3000	Interstitial	Yes	No	26	Fetal death	
Davenport *et al.* (2004)[104]	1	CPAM	19	No	31	NA	NA	Interstitial	Yes	Yes	37	Neonatal death	
Ong *et al.* (2006)[117]	1	CPAM	21	No		45	1683	Interstitial	No	Yes	37	Alive	Sequestrectomy
Oepkes *et al.* (2007)[118]	1	BPS	23	No		50	1695	Vascular	No	Yes	39	Alive	No
Ruano *et al.* (2007)[119]	1	BPS	29	No		35	1500	Vascular	Yes	Yes	38	Alive	Sequestrectomy
Cavoretto *et al* (2008)[98]	9	BPS	31	No		30–50	NA	Vascular	No	NA	38	Alive	Sequestrectomy
		BPS	30	No		30–50	NA	Vascular	No	NA	38	Alive	Sequestrectomy
		BPS	32	No		30–50	NA	Vascular	No	NA	34	Alive	No
		BPS	27	No		30–50	NA	Vascular	No	NA	41	Alive	No
		BPS	24	No		30–50	NA	Vascular	No	NA	40	Alive	No
		BPS	31	No		30–50	NA	Vascular	No	NA	34	Alive	Sequestrectomy
		BPS	23	No		30–50	NA	Vascular	No	NA	35	Alive	Sequestrectomy
		BPS	28	No		30–50	NA	Vascular	No	NA	39	Alive	Sequestrectomy
		CPAM	19	No	31	NA	NA	Interstitial	Yes	Yes	37	Neonatal death	
Witlox *et al.* (2009)[99]	1	BPS	23	No		20	1310	Vascular	No	Yes	41	Alive	No
Rammos *et al.* (2010)[121]	2	BPS	30	Yes		NA	NA	Vascular	Yes	Yes	NA	Alive	Sequestrectomy
		BPS	31	Yes	32	NA	NA	Vascular	Yes	No	NA	Alive	Sequestrectomy
Ruano *et al.* (2012)[111]	6	BPS	24	No	26	30	1450	Vascular	Yes	Yes	36	Alive	No
		BPS	28	No		30	1360	Vascular	Yes	Yes	39	Alive	No
		BPS	29	No		40	1610	Interstitial	Yes	No	30	Fetal death	
		CPAM	23	No		30	1530	Interstitial	Yes	No	25	Fetal death	
		CPAM	21	No	25	30	1420	Interstitial	Yes	No	29	Neonatal death	
		CPAM	24	No		30	1310	Interstitial	Yes	Yes	34	Neonatal death	
Baud *et al.* (2013)[107]	1	BPS/CPAM	19	Yes		50	2963	Vascular	No	Yes	39	Alive	Lobectomy
Fetal bronchoscopy													
Kohl *et al.* (2009)[123]	1	LA	22	No		NA	NA	Atretic region			31	Alive	EXIT
Martinez *et al.* (2013)[124]	1	BA	27	No		NA	10	Atretic region			38	Alive	Inf. lobectomy
Cruz-Martinez *et al.* (2014)[125]	1	CPAM	30	No	22	NA	10	BM			39	Alive	No

NA, not available; CCAM, congenital cyst adenomatoid malformation; BPS, bronchopulmonary sequestration; GA, gestational age; ND YAG, neomymium-doped yttrium aluminum garnet.

2-mm fetoscope confirmed laryngeal atresia and tracheal decompression was achieved by Nd : YAG laser vaporization.[123] Delivery by EXIT procedure was indicated at 31.1 weeks of gestation because of preeclampsia. After discharge from the hospital at four months of age, CPAP was the only necessary treatment. Similar procedures were performed under epidural anaesthesia in the cases of a BA[124] and a hydropic CPAM,[125] at 27 and 30 weeks of gestation respectively. The bronchial membranes were perforated with the laser fiber at a power setting of 10 W via fetal bronchoscopy.[124,125] Both fetuses were born at term. Only one required an inferior lobectomy.[124]

In conclusion, laser therapy seems to be a promising option to occlude the vascular supply of a hydropic BPS or to restore tracheobronchic airways in cases of obstruction/atresia. In hydropic CPAM, steroid treatment should always be attempted before any invasive procedure. The only indications for which laser therapy should be discussed are lung masses with associated high-output failure. Further research is needed to optimize these approaches, and parents should be informed of the experimental nature of these treatments.

DISCUSSION

Amniotic band syndrome, chorioangiomas, low urinary tract obstructions, SCTs and chest masses are rare diseases. A minority of cases can evolve to severe fetal and neonatal complications. In this article, we reviewed minimally invasive laser techniques to reverse these pathologies, either by using fetoscopic or ultrasound-guided approaches.

We must acknowledge several limitations of our review. First, we do not provide a level of evidence that supports laser therapy over other treatment options. Except for cases of TTTS, fetal laser therapy has not been evaluated in randomized controlled trials for other pathologies. Second, most cases described here are based on case reports or small case series, and reporting or investigator bias are thus not excluded. Third, a better selection criteria for fetal laser therapy needs to be defined. Fourth, unsuccessful attempts or complications have likely gone unreported. Finally, there is poor follow-up beyond the neonatal period for patients treated with laser therapy or other treatment options. Despite these limitations, growing evidence suggest that fetal laser therapy might be considered as a treatment option in pathologies other than TTTS.

Considering the difficulty of performing optimally designed trials,[126] parents should be extensively counseled that the interventions described here remain experimental and should only be performed in select fetal therapy centers. *In utero* procedures should only be offered after a multidisciplinary review of the fetal findings. The pediatric surgical team should ideally participate in these fetal laser therapy procedures. Fetal laser therapy has been used experimentally in certain conditions for highly selected cases. It is unclear whether the reported findings, which are subject to reporting bias, are generalizable. Careful evaluation in well delineated research settings, reporting of both positive and negative results, as well as a re-evaluation of the natural history of many conditions in an era of improved neonatal care, are highly needed before any benefit can be implied.

ACKNOWLEDGEMENTS

We warmly thank Maud de Rham, Dony-So Alissa Ying Ying, Sam Vasilevsky, Kirsten Niles and Karine Lepigeon for computer assistance and/or critical review of the manuscript.

WHAT'S ALREADY KNOWN ABOUT THIS TOPIC?

- Pathologies other than the largely reported twin-to-twin transfusion syndrome might benefit from endoscopic or ultrasound-guided laser therapy.

WHAT DOES THIS STUDY ADD?

- We describe here emerging and promising applications of fetal laser therapy in ABS, lower urinary tract obstructions and fetal or placental tumors.
- Strict selection criteria and long-term follow-up of theses rare cases are needed to prove the value of such therapy.

REFERENCES

1. Chalouhi GE, Marangoni MA, Quibel T, *et al.* Active management of selective intrauterine growth restriction with abnormal Doppler in monochorionic diamniotic twin pregnancies diagnosed in the second trimester of pregnancy. Prenat Diagn 2013;33:109–15.
2. Chalouhi GE, Essaoui M, Stirnemann J, *et al.* Laser therapy for twin-to-twin transfusion syndrome (TTTS). Prenat Diagn 2011;31:637–46.
3. van Mieghem T, Baud D, Devlieger R, *et al.* Minimally invasive fetal therapy. Best Pract Res Clin Obstet Gynaecol 2012;26:711–25.
4. Wimalasundera RC. Selective reduction and termination of multiple pregnancies. Semin Fetal Neonatal Med 2010;15:327–35.
5. Spadola AC, Simpson LL. Selective termination procedures in monochorionic pregnancies. Semin Perinatol 2005;29:330–7.
6. Lewi L, Gratacos E, Ortibus E, *et al.* Pregnancy and infant outcome of 80 consecutive cord coagulations in complicated monochorionic multiple pregnancies. Am J Obstet Gynecol 2006;194:782–9.
7. Berg C, Holst D, Mallmann MR, *et al.* Early vs late intervention in twin reversed arterial perfusion sequence. Ultrasound Obstet Gynecol 2014;43:60–4.
8. Pagani G, D'Antonio F, Khalil A, *et al.* Intrafetal laser treatment for twin reversed arterial perfusion sequence: cohort study and meta-analysis. Ultrasound Obstet Gynecol 2013;42:6–14.
9. Scheier M, Molina FS. Outcome of twin reversed arterial perfusion sequence following treatment with interstitial laser: a retrospective study. Fetal Diagn Ther 2012;31:35–41.
10. Kohl T. Minimally invasive fetoscopic interventions: an overview in 2010. Surg Endosc 2010;24:2056–67.
11. Garza A, Cordero JF, Mulinare J. Epidemiology of the early amnion rupture spectrum of defects. Am J Dis Child 1988;142:541–4.
12. Richter J, Wergeland H, *et al.* Fetoscopic release of an amniotic band with risk of amputation: case report and review of the literature. Fetal Diagn Ther 2012;31:134–7.
13. Tadmor OP, Kreisberg GA, Achiron R, *et al.* Limb amputation in amniotic band syndrome: serial ultrasonographic and Doppler observations. Ultrasound Obstet Gynecol 1997;10:312–5.
14. Pedersen TK, Thomsen SG. Spontaneous resolution of amniotic bands. Ultrasound Obstet Gynecol 2001;18:673–4.
15. Sentilhes L, Verspyck E, Eurin D, *et al.* Favourable outcome of a tight constriction band secondary to amniotic band syndrome. Prenat Diagn 2004;24:198–201.
16. Crombleholme TM, Dirkes K, Whitney TM, *et al.* Amniotic band syndrome in fetal lambs. I: fetoscopic release and morphometric outcome. J Pediatr Surg 1995;30:974–8.

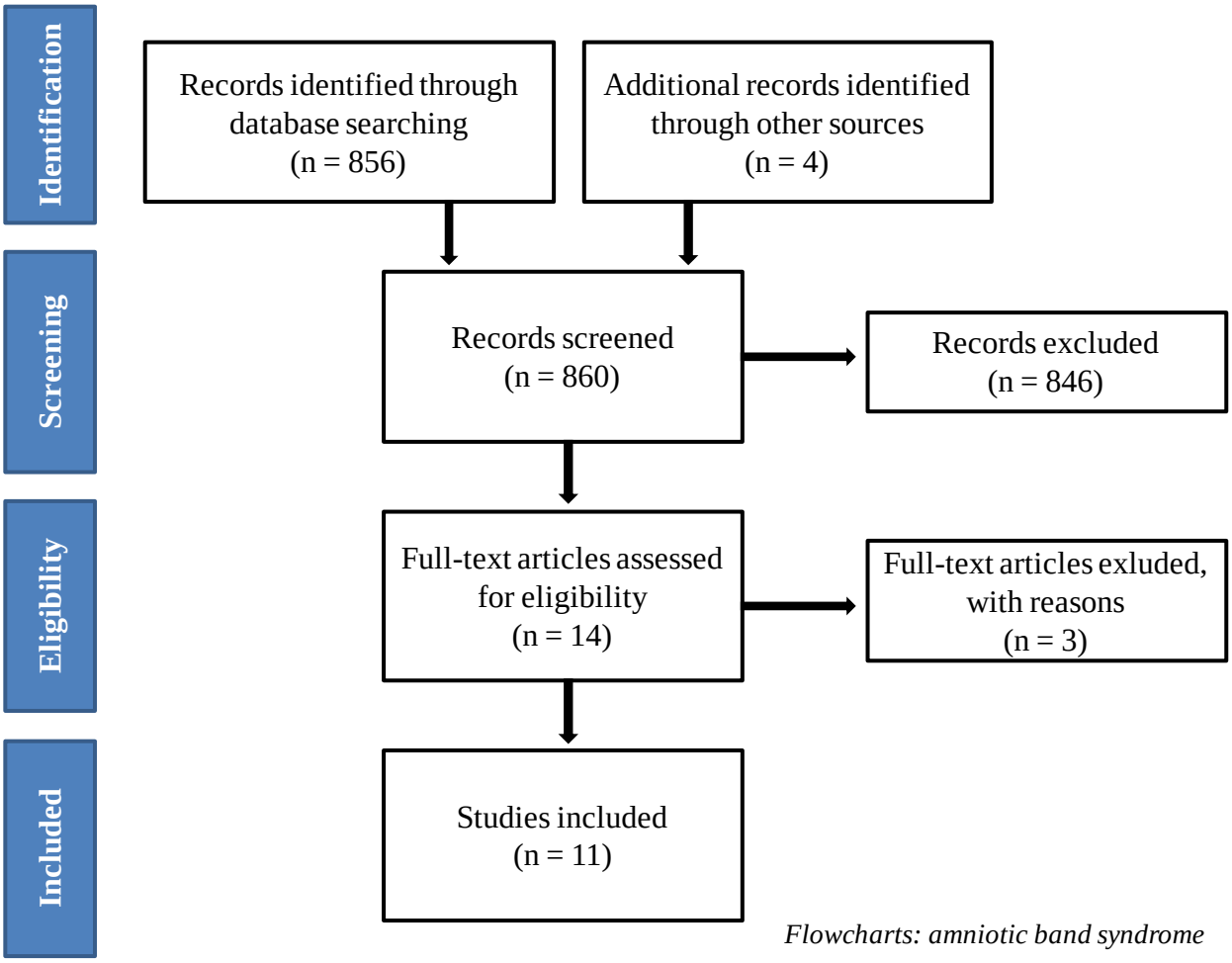
17. Soldado F, Aguirre M, Peiro JL, *et al.* Fetoscopic release of extremity amniotic bands with risk of amputation. J Pediatr Orthop 2009;29:290–3.
18. Quintero RA, Morales WJ, Phillips J, *et al.* In utero lysis of amniotic bands. Ultrasound Obstet Gynecol 1997;10:316–20.
19. Peiro JL, Carreras E, Soldado F, *et al.* Fetoscopic release of umbilical cord amniotic band in a human fetus. Ultrasound Obstet Gynecol 2009;33:232–4.
20. Keswani SG, Johnson MP, Adzick NS, *et al.* In utero limb salvage: fetoscopic release of amniotic bands for threatened limb amputation. J Pediatr Surg 2003;38:848–51.
21. Keswani SG, Crombleholme TM, Rychik J, *et al.* Impact of continuous intraoperative monitoring on outcomes in open fetal surgery. Fetal Diagn Ther 2005;20:316–20.
22. Husler MR, Wilson RD, Horii SC, *et al.* When is fetoscopic release of amniotic bands indicated? review of outcome of cases treated in utero and selection criteria for fetal surgery. Prenat Diagn 2009;29:457–63.
23. Soldado F, Aguirre M, Peiro JL, *et al.* Fetal surgery of extremity amniotic bands: an experimental model of in utero limb salvage in fetal lamb. J Pediatr Orthop 2009;29:98–102.
24. Ronderos-Dumit D, Briceno F, Navarro H, Sanchez N. Endoscopic release of limb constriction rings in utero. Fetal Diagn Ther 2006;21:255–8.
25. Assaf R, Llanes A, Chmait R. In utero release of constriction amniotic bands via blunt dissection. Fetal Pediatr Pathol 2012;31:25–9.
26. Javadian P, Shamshirsaz AA, Haeri S, *et al.* Perinatal outcome after fetoscopic release of amniotic bands: a single-center experience and review of the literature. Ultrasound Obstet Gynecol 2013;42:449–55.
27. Derderian SC, Iqbal CW, Goldstein R, *et al.* Fetoscopic approach to amniotic band syndrome. J Pediatr Surg 2014;49:359–62.
28. Rodrigues A, Araujo C, Carvalho R, *et al.* Limb constriction secondary to pseudoamniotic band syndrome after selective fetoscopic laser surgery: report of a case with a favorable outcome. Fetal Diagn Ther 2012;32:288–91.
29. Winer N, Salomon LJ, Essaoui M, *et al.* Pseudoamniotic band syndrome: a rare complication of monochorionic twins with fetofetal transfusion syndrome treated by laser coagulation. Am J Obstet Gynecol 2008;198:393.e1–5.
30. Sepulveda W, Alcalde JL, Schnapp C, Bravo M. Perinatal outcome after prenatal diagnosis of placental chorioangioma. Obstet Gynecol 2003;102:1028–33.
31. Jauniaux E, Ogle R. Color Doppler imaging in the diagnosis and management of chorioangiomas. Ultrasound Obstet Gynecol 2000;15:463–7.
32. Sepulveda W, Aviles G, Carstens E, *et al.* Placental chorioangioma. Ultrasound Obstet Gynecol 2000;16:597–8.
33. Haak MC, Oosterhof H, Mouw RJ, *et al.* Pathophysiology and treatment of fetal anemia due to placental chorioangioma. Ultrasound Obstet Gynecol 1999;14:68–70.
34. Hamil KG, Liu Q, Sivashanmugam P, *et al.* LCN6, a novel human epididymal lipocalin. Reprod Biol Endocrinol 2003;1:112.
35. Escribano D, Galindo A, Arbues J, *et al.* Prenatal management of placental chorioangioma: value of the middle cerebral artery peak systolic velocity. Fetal Diagn Ther 2006;21:489–93.
36. As AK, Hagen P, Webb JB, Wijesinghe D. Therapeutic amniodrainage in chorioangioma. J Obstet Gynaecol 1997;17:169–70.
37. Nicolini U, Zuliani G, Caravelli E, *et al.* Alcohol injection: a new method of treating placental chorioangiomas. Lancet 1999;353:1674–5.
38. Wanapirak C, Tongsong T, Sirichotiyakul S, Chanprapaph P. Alcoholization: the choice of intrauterine treatment for chorioangioma. J Obstet Gynaecol Res 2002;28:71–5.
39. Deren O, Ozyuncu O, Onderoglu LS, Durukan T. Alcohol injection for the intrauterine treatment of chorioangioma in a pregnancy with transfusion resistant fetal anemia: a case report. Fetal Diagn Ther 2007;22:203–5.
40. Babic I, Tulbah M, Kurdi W. Antenatal embolization of a large placental chorioangioma: a case report. J Med Case Rep 2012;6:183.
41. Lau TK, Yu SC, Leung TY, *et al.* Prenatal embolisation of a large chorioangioma using enbucrilate. BJOG 2005;112:1002–4.
42. Bolla DK, Kettenbach, J, Vial, Y, *et al.* Percutaneous embolization of a giant placental chorioangioma with n-Butyl-2-Cyanoacrylate:a case report and review of the literature. Am J Ultrasound 2014;1:25–31.
43. Gajewska K, Herinckx A, Holoye A, *et al.* Antenatal embolization of a large chorioangioma by percutaneous Glubran 2 injection. Ultrasound Obstet Gynecol 2010;36:773–5.
44. Lau TK, Leung TY, Yu SC, *et al.* Prenatal treatment of chorioangioma by microcoil embolisation. BJOG 2003;110:70–3.
45. Quintero RA, Reich H, Romero R, *et al.* In utero endoscopic devascularization of a large chorioangioma. Ultrasound Obstet Gynecol 1996;8:48–52.
46. Bhide A, Prefumo F, Sairam S, *et al.* Ultrasound-guided interstitial laser therapy for the treatment of placental chorioangioma. Obstet Gynecol 2003;102:1189–91.
47. Quarello E, Bernard JP, Leroy B, Ville Y. Prenatal laser treatment of a placental chorioangioma. Ultrasound Obstet Gynecol 2005;25:299–301.
48. Bhide A, Prefumo F, Moore J, *et al.* Placental edge to internal os distance in the late third trimester and mode of delivery in placenta praevia. BJOG 2003;110:860–4.
49. Sepulveda W, Wong AE, Herrera L, *et al.* Endoscopic laser coagulation of feeding vessels in large placental chorioangiomas: report of three cases and review of invasive treatment options. Prenat Diagn 2009;29:201–6.
50. Zanardini C, Papageorghiou A, Bhide A, Thilaganathan B. Giant placental chorioangioma: natural history and pregnancy outcome. Ultrasound Obstet Gynecol 2010;35:332–6.
51. Bermudez C, Luengas O, Perez-Wulff J, *et al.* Management of a placental chorioangioma with endoscopic devascularization and intrauterine transfusions. Ultrasound Obstet Gynecol 2007;29:97–8.
52. Mendez-Figueroa H, Papanna R, Popek EJ, *et al.* Endoscopic laser coagulation following amnioreduction for the management of a large placental chorioangioma. Prenat Diagn 2009;29:1277–8.
53. Jones K, Tierney K, Grubbs BH, *et al.* Fetoscopic laser photocoagulation of feeding vessels to a large placental chorioangioma following fetal deterioration after amnioreduction. Fetal Diagn Ther 2012;31:191–5.
54. Jhun KM, Nassar P, Chen TS, *et al.* Giant chorioangioma treated in utero via laser of feeding vessels with subsequent development of multifocal infantile hemangiomas. Fetal Pediatr Pathol 2015;34(1):1–8, DOI: 10.3109/15513815.2014.925018.
55. Muller Brochut AC, Thomann D, Kluwe W, *et al.* Fetal megacystis: experience of a single tertiary center in Switzerland over 20 years. Fetal Diagn Ther 2014;36:215–22.
56. Ruano R. Fetal surgery for severe lower urinary tract obstruction. Prenat Diagn 2011;31:667–74.
57. Morris RK, Malin GL, Khan KS, Kilby MD. Systematic review of the effectiveness of antenatal intervention for the treatment of congenital lower urinary tract obstruction. BJOG 2010;117:382–90.
58. Morris RK, Kilby MD. Long-term renal and neurodevelopmental outcome in infants with LUTO, with and without fetal intervention. Early Hum Dev 2011;87:607–10.
59. Morris RK, Malin GL, Quinlan-Jones E, *et al.* Percutaneous vesicoamniotic shunting versus conservative management for fetal lower urinary tract obstruction (PLUTO): a randomised trial. Lancet 2013;382:1496–506.
60. Morris RK, Kilby MD. An overview of the literature on congenital lower urinary tract obstruction and introduction to the PLUTO trial: percutaneous shunting in lower urinary tract obstruction. Aust N Z J Obstet Gynaecol 2009;49:6–10.
61. Sananes N, Favre R, Koh CJ, *et al.* Urological fistulas after fetal cystoscopic laser ablation of posterior urethral valves—surgical technical aspects. Ultrasound Obstet Gynecol 2015;45(2):183–9, DOI: 10.1002/uog.13405.
62. Kilby MD, Morris RK. Fetal therapy for the treatment of congenital bladder neck obstruction. Nat Rev Urol 2014;11:412–9.
63. Morris RK, Ruano R, Kilby MD. Effectiveness of fetal cystoscopy as a diagnostic and therapeutic intervention for lower urinary tract obstruction: a systematic review. Ultrasound Obstet Gynecol 2011;37:629–37.
64. Welsh A, Agarwal S, Kumar S, *et al.* Fetal cystoscopy in the management of fetal obstructive uropathy: experience in a single European centre. Prenat Diagn 2003;23:1033–41.
65. Ruano R, Yoshisaki CT, Salustiano EM, *et al.* Early fetal cystoscopy for first-trimester severe megacystis. Ultrasound Obstet Gynecol 2011;37:696–701.

66. Quintero RA, Shukla AR, Homsy YL, Bukkapatnam R. Successful in utero endoscopic ablation of posterior urethral valves: a new dimension in fetal urology. Urology 2000;55:774.
67. Holmes N, Harrison MR, Baskin LS. Fetal surgery for posterior urethral valves: long-term postnatal outcomes. Pediatrics 2001;108:E7.
68. Favre R, Kohler M, Gasser B, *et al.* Early fetal megacystis between 11 and 15 weeks of gestation. Ultrasound Obstet Gynecol 1999;14:402–6.
69. Holmes M, Stewart J, Rice M. Flexible cystoscopy: is the volume and content of the urethral gel critical? J Endourol 2001;15:855–8.
70. Quintero RA, Homsy Y, Bornick PW, *et al.* In-utero treatment of fetal bladder-outlet obstruction by a ureterocele. Lancet 2001;357:1947–8.
71. Quintero RA, Hume R, Smith C, *et al.* Percutaneous fetal cystoscopy and endoscopic fulguration of posterior urethral valves. Am J Obstet Gynecol 1995;172:206–9.
72. Quintero RA, Johnson MP, Romero R, *et al.* In-utero percutaneous cystoscopy in the management of fetal lower obstructive uropathy. Lancet 1995;346:537–40.
73. Ruano R, Duarte S, Bunduki V, *et al.* Fetal cystoscopy for severe lower urinary tract obstruction—initial experience of a single center. Prenat Diagn 2010;30:30–9.
74. Ruano R, Yoshizaki CT, Giron AM, *et al.* Cystoscopic placement of transurethral stent in a fetus with urethral stenosis. Ultrasound Obstet Gynecol 2014;44:238–40.
75. Sago H, Hayashi S, Chiba T, *et al.* Endoscopic fetal urethrotomy for anterior urethral valves: a preliminary report. Fetal Diagn Ther 2008;24:92–5.
76. Soothill PW, Bartha JL, Tizard J. Ultrasound-guided laser treatment for fetal bladder outlet obstruction resulting from ureterocele. Am J Obstet Gynecol 2003;188:1107–8.
77. Gucciardo L, Uyttebroek A, De Wever I, *et al.* Prenatal assessment and management of sacrococcygeal teratoma. Prenat Diagn 2011;31:678–88.
78. Wilson RD, Hedrick H, Flake AW, *et al.* Sacrococcygeal teratomas: prenatal surveillance, growth and pregnancy outcome. Fetal Diagn Ther 2009;25:15–20.
79. Iacovella C, Chandrasekaran N, Khalil A, *et al.* Fetal and placental vascular tumors: persistent fetal hyperdynamic status predisposes to poorer long-term neurodevelopmental outcome. Ultrasound Obstet Gynecol 2014;43:658–61.
80. Benachi A, Durin L, Maurer SV, *et al.* Prenatally diagnosed sacrococcygeal teratoma: a prognostic classification. J Pediatr Surg 2006;41:1517–21.
81. Holcroft CJ, Blakemore KJ, Gurewitsch ED, *et al.* Large fetal sacrococcygeal teratomas: could early delivery improve outcome? Fetal Diagn Ther 2008;24:55–60.
82. Roybal JL, Moldenhauer JS, Khalek N, *et al.* Early delivery as an alternative management strategy for selected high-risk fetal sacrococcygeal teratomas. J Pediatr Surg 2011;46:1325–32.
83. Geipel A, Berg C. Re: Minimally invasive therapy for fetal sacrococcygeal teratoma: case series and systematic review of the literature. T. Van Mieghem, A. Al-Ibrahim, J. Deprest, L. Lewi, J. C. Langer, D. Baud, K. O'Brien, R. Beecroft, R. Chaturvedi, E. Jaeggi, J. Fish and G. Ryan. Ultrasound Obstet Gynecol 2014;43:611-619. Ultrasound Obstet Gynecol 2014;43:609.
84. Van Mieghem T, Al-Ibrahim A, Deprest J, *et al.* Minimally invasive therapy for fetal sacrococcygeal teratoma: case series and systematic review of the literature. Ultrasound Obstet Gynecol 2014;43:611–9.
85. Grethel EJ, Wagner AJ, Clifton MS, *et al.* Fetal intervention for mass lesions and hydrops improves outcome: a 15-year experience. J Pediatr Surg 2007;42:117–23.
86. McCann SM, Emery SP, Vallejo MC. Anesthetic management of a parturient with fetal sacrococcygeal teratoma and mirror syndrome complicated by elevated hCG and subsequent hyperthyroidism. J Clin Anesth 2009;21:521–4.
87. Ibele A, Flake A, Shaaban A. Survival of a profoundly hydropic fetus with a sacrococcygeal teratoma delivered at 27 weeks of gestation for maternal mirror syndrome. J Pediatr Surg 2008;43:e17–20.
88. Adzick NS, Thom EA, Spong CY, *et al.* A randomized trial of prenatal versus postnatal repair of myelomeningocele. N Engl J Med 2011;364:993–1004.
89. Hedrick HL, Flake AW, Crombleholme TM, *et al.* Sacrococcygeal teratoma: prenatal assessment, fetal intervention, and outcome. J Pediatr Surg 2004;39:430–8; discussion 30–8.
90. Adzick NS. Open fetal surgery for life-threatening fetal anomalies. Semin Fetal Neonatal Med 2010;15:1–8.
91. Lam YH, Tang MH, Shek TW. Thermocoagulation of fetal sacrococcygeal teratoma. Prenat Diagn 2002;22:99–101.
92. Paek BW, Jennings RW, Harrison MR, *et al.* Radiofrequency ablation of human fetal sacrococcygeal teratoma. Am J Obstet Gynecol 2001;184:503–7.
93. Perrotin A, Isingrini M, Souchay C, *et al.* Episodic feeling-of-knowing accuracy and cued recall in the elderly: evidence for double dissociation involving executive functioning and processing speed. Acta Psychol (Amst) 2006;122:58–73.
94. Makin EC, Hyett J, Ade-Ajayi N, *et al.* Outcome of antenatally diagnosed sacrococcygeal teratomas: single-center experience (1993–2004). J Pediatr Surg 2006;41:388–93.
95. Hecher K, Hackeloer BJ. Intrauterine endoscopic laser surgery for fetal sacrococcygeal teratoma. Lancet 1996;347:470.
96. Ruano R, Duarte S, Zugaib M. Percutaneous laser ablation of sacrococcygeal teratoma in a hydropic fetus with severe heart failure—too late for a surgical procedure? Fetal Diagn Ther 2009;25:26–30.
97. Ding J, Chen Q, Stone P. Percutaneous laser photocoagulation of tumour vessels for the treatment of a rapidly growing sacrococcygeal teratoma in an extremely premature fetus. J Matern Fetal Neonatal Med 2010;23:1516–8.
98. Cavoretto P, Molina F, Poggi S, *et al.* Prenatal diagnosis and outcome of echogenic fetal lung lesions. Ultrasound Obstet Gynecol 2008;32:769–83.
99. Witlox RS, Lopriore E, Oepkes D. Prenatal interventions for fetal lung lesions. Prenat Diagn 2011;31:628–36.
100. Khalek N, Johnson MP. Management of prenatally diagnosed lung lesions. Semin Pediatr Surg 2013;22:24–9.
101. Osborn AJ, Baud D, Macarthur AJ, *et al.* Multidisciplinary perinatal management of the compromised airway on placental support: lessons learned. Prenat Diagn 2013;33:1080–7.
102. Ruano R, Benachi A, Aubry MC, *et al.* Prenatal diagnosis of pulmonary sequestration using three-dimensional power Doppler ultrasound. Ultrasound Obstet Gynecol 2005;25:128–33.
103. Hung JH, Shen SH, Guo WY, *et al.* Prenatal diagnosis of pulmonary sequestration by ultrasound and magnetic resonance imaging. J Chin Med Assoc 2008;71:53–7.
104. Davenport M, Warne SA, Cacciaguerra S, *et al.* Current outcome of antenally diagnosed cystic lung disease. J Pediatr Surg 2004;39:549–56.
105. Raychaudhuri P, Pasupati A, James A, *et al.* Prospective study of antenatally diagnosed congenital cystic adenomatoid malformations. Pediatr Surg Int 2011;27:1159–64.
106. Bunduki V, Ruano R, da Silva MM, *et al.* Prognostic factors associated with congenital cystic adenomatoid malformation of the lung. Prenat Diagn 2000;20:459–64.
107. Baud D, Windrim R, Kachura JR, *et al.* Minimally invasive fetal therapy for hydropic lung masses: three different approaches and review of the literature. Ultrasound Obstet Gynecol 2013;42:440–8.
108. Peranteau WH, Wilson RD, Liechty KW, *et al.* Effect of maternal betamethasone administration on prenatal congenital cystic adenomatoid malformation growth and fetal survival. Fetal Diagn Ther 2007;22:365–71.
109. Curran PF, Jelin EB, Rand L, *et al.* Prenatal steroids for microcystic congenital cystic adenomatoid malformations. J Pediatr Surg 2010;45:145–50.
110. Schrey S, Kelly EN, Langer JC, *et al.* Fetal thoracoamniotic shunting for large macrocystic congenital cystic adenomatoid malformations of the lung. Ultrasound Obstet Gynecol 2012;39:515–20.
111. Ruano R, da Silva MM, Salustiano EM, *et al.* Percutaneous laser ablation under ultrasound guidance for fetal hyperechogenic microcystic lung lesions with hydrops: a single center cohort and a literature review. Prenat Diagn 2012;32:1127–32.
112. Nicolini U, Cerri V, Groli C, *et al.* A new approach to prenatal treatment of extralobar pulmonary sequestration. Prenat Diagn 2000;20:758–60.
113. Bermudez C, Perez-Wulff J, Arcadipane M, *et al.* Percutaneous fetal sclerotherapy for congenital cystic adenomatoid malformation of the lung. Fetal Diagn Ther 2008;24:237–40.
114. Bermudez C, Perez-Wulff J, Bufalino G, *et al.* Percutaneous ultrasound-guided sclerotherapy for complicated fetal intralobar bronchopulmonary sequestration. Ultrasound Obstet Gynecol 2007;29:586–9.
115. Fortunato SJL, Daniell JF, Ismael S. Intrauterine laser ablationof a fetal cystic adenomatoid malformation with hydrops: the application of

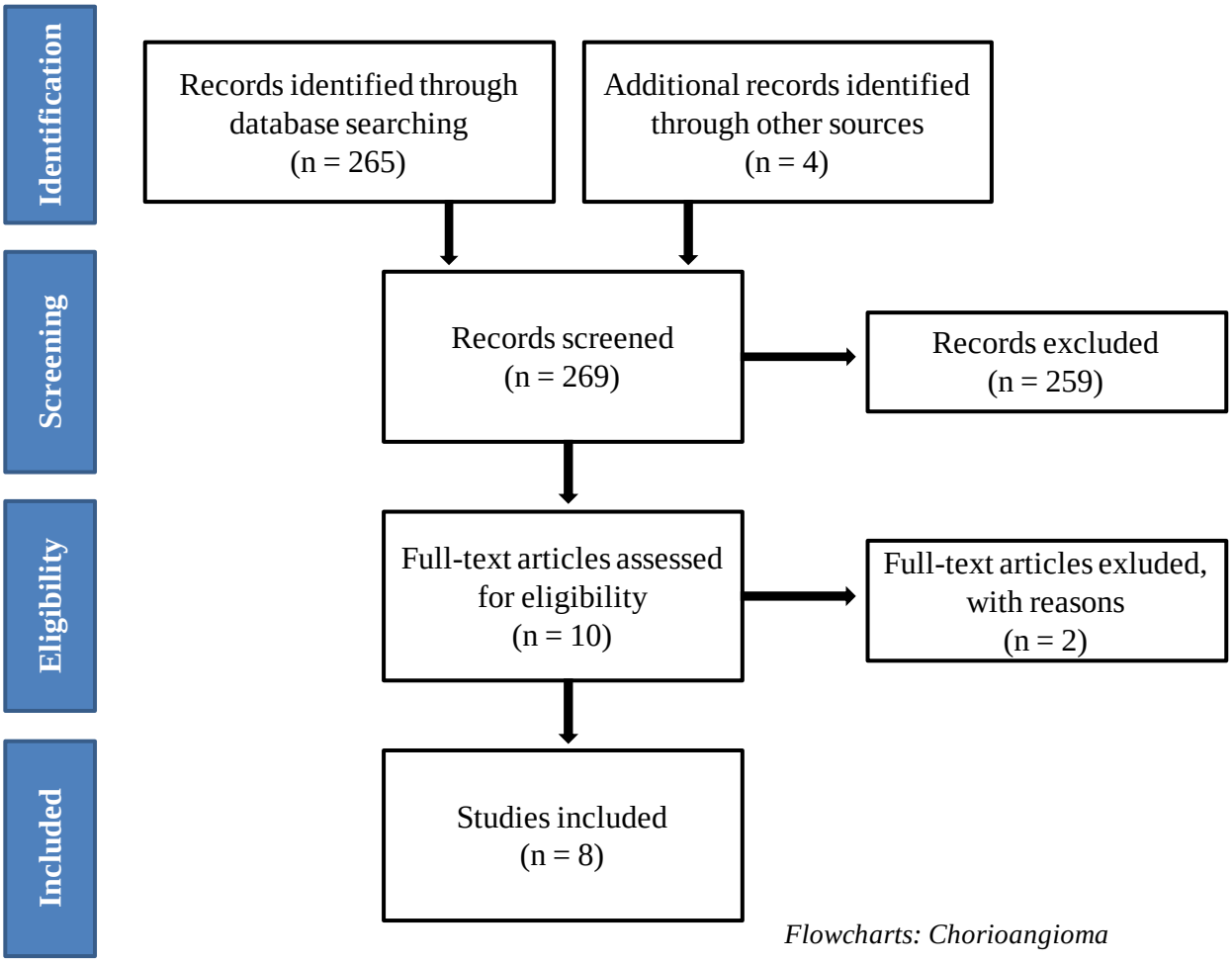
minimally invasive surgical techniques to fetal surgery. Am J Obstet Gynecol 1997;177.
116. Bruner JP, Jarnagin BK, Reinisch L. Percutaneous laser ablation of fetal congenital cystic adenomatoid malformation: too little, too late? Fetal Diagn Ther 2000;15:359–63.
117. Ong SS, Chan SY, Ewer AK, *et al.* Laser ablation of fetal microcystic lung lesion: successful outcome and rationale for its use. Fetal Diagn Ther 2006;21:471–4.
118. Oepkes D, Devlieger R, Lopriore E, Klumper FJ. Successful ultrasound-guided laser treatment of fetal hydrops caused by pulmonary sequestration. Ultrasound Obstet Gynecol 2007;29:457–9.
119. Ruano R, de A Pimenta EJ, Marques da Silva M, *et al.* Percutaneous intrauterine laser ablation of the abnormal vessel in pulmonary sequestration with hydrops at 29 weeks' gestation. J Ultrasound Med 2007;26:1235–41.
120. Witlox RS, Lopriore E, Walther FJ, *et al.* Single-needle laser treatment with drainage of hydrothorax in fetal bronchopulmonary sequestration with hydrops. Ultrasound Obstet Gynecol 2009;34:355–7.
121. Rammos KS, Foroulis CN, Rammos CK, Andreou A. Prenatal interventional and postnatal surgical therapy of extralobar pulmonary sequestration. Interact Cardiovasc Thorac Surg 2010;10:634–5.
122. Tsao K, Hawgood S, Vu L, *et al.* Resolution of hydrops fetalis in congenital cystic adenomatoid malformation after prenatal steroid therapy. J Pediatr Surg 2003;38:508–10.
123. Kohl T, Van de Vondel P, Stressig R, *et al.* Percutaneous fetoscopic laser decompression of congenital high airway obstruction syndrome (CHAOS) from laryngeal atresia via a single trocar—current technical constraints and potential solutions for future interventions. Fetal Diagn Ther 2009;25:67–71.
124. Martinez JM, Prat J, Gomez O, *et al.* Decompression through tracheobronchial endoscopy of bronchial atresia presenting as massive pulmonary tumor: a new indication for fetoscopic surgery. Fetal Diagn Ther 2013;33:69–74.
125. Cruz-Martinez R, Mendez A, Perez-Garcilita O, *et al.* Fetal bronchoscopy as a useful procedure in a case with prenatal diagnosis of congenital microcystic adenomatoid malformation. Fetal Diagn Ther 2015;37(1):75–80, DOI: 10.1159/000361015.
126. Van Mieghem T, Ryan G. The PLUTO trial: a missed opportunity. Lancet 2013;382:1471–3.

SUPPORTING INFORMATION

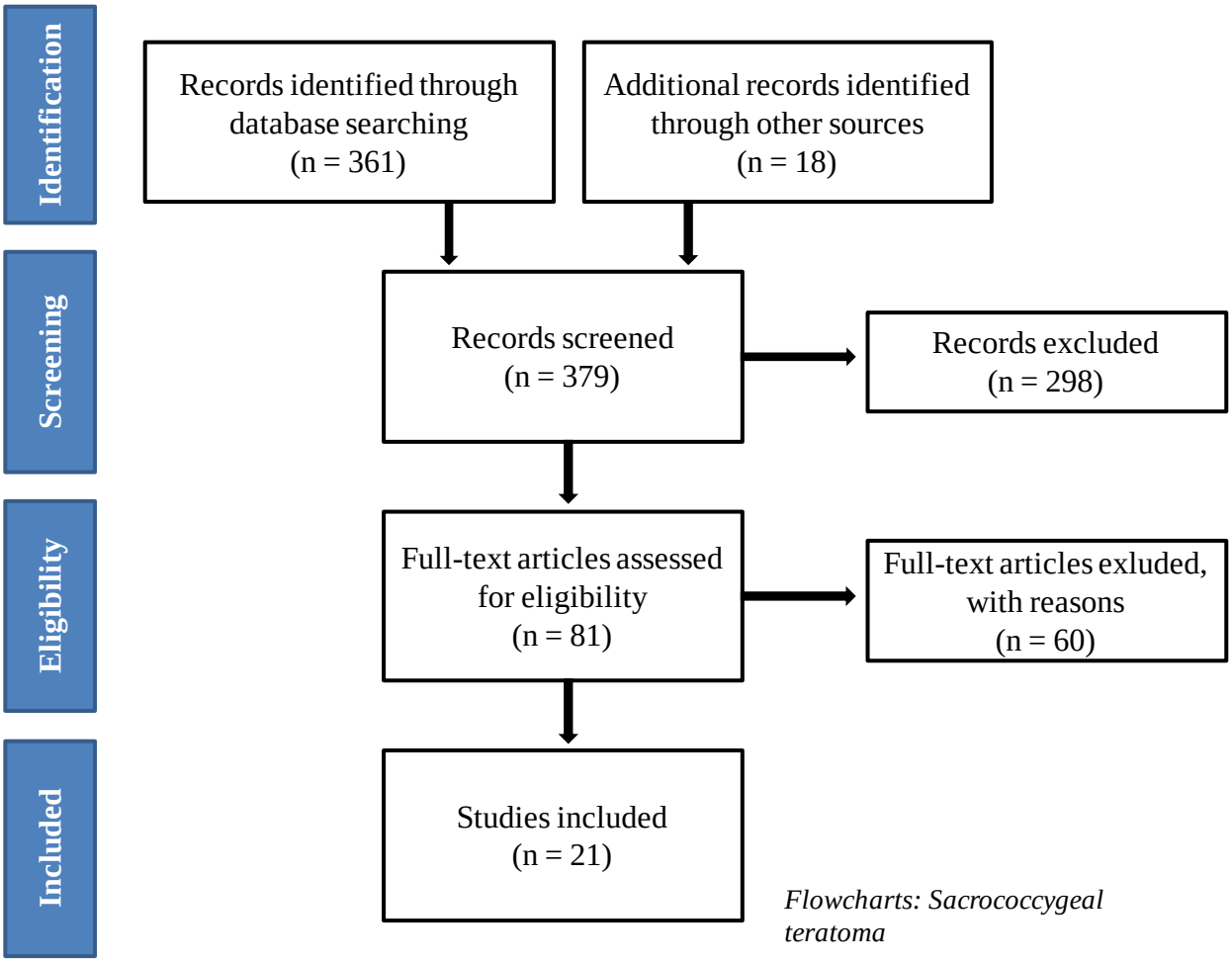
Additional supporting information may be found in the online version of this article at the publisher's web site.



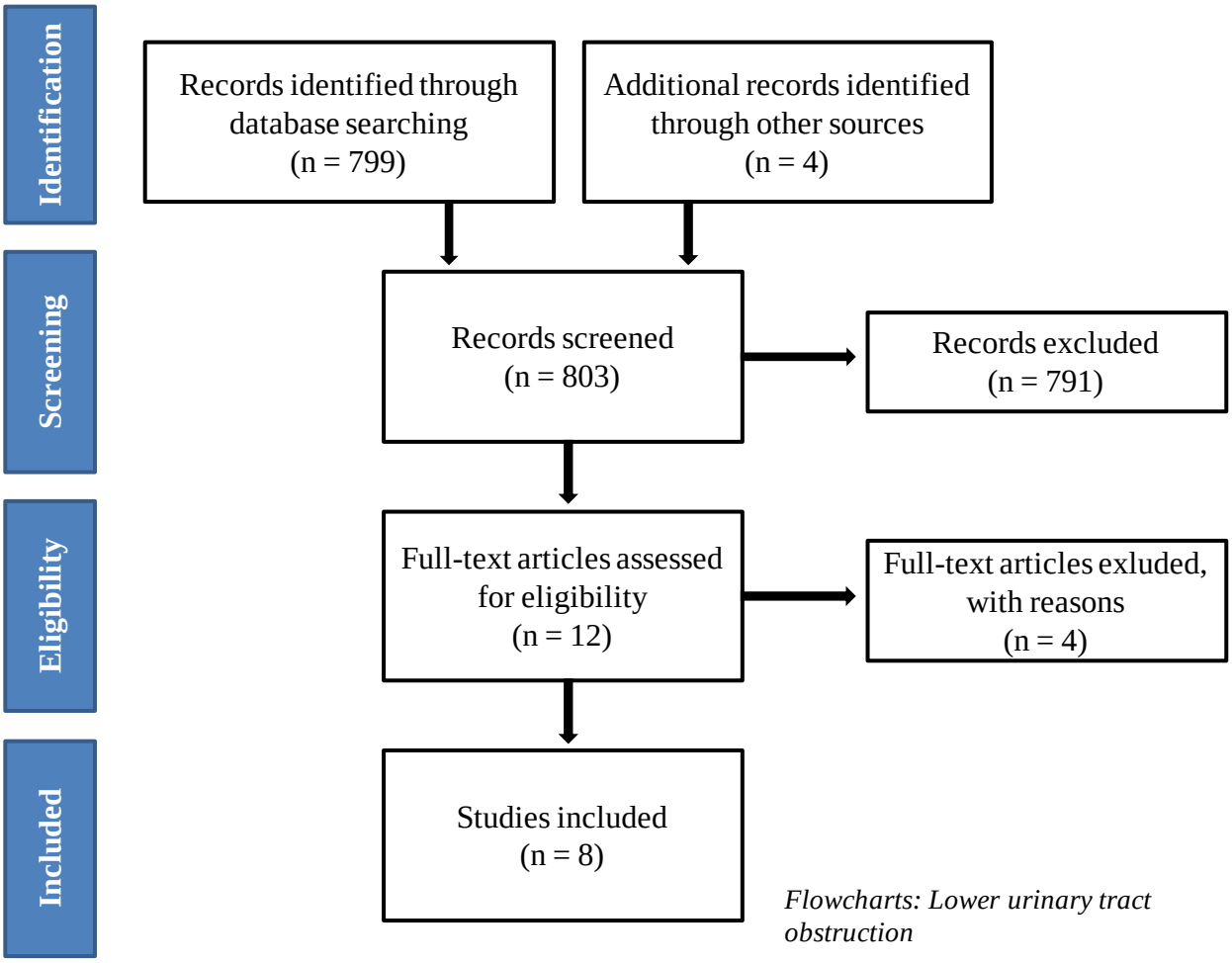
Flowcharts: amniotic band syndrome



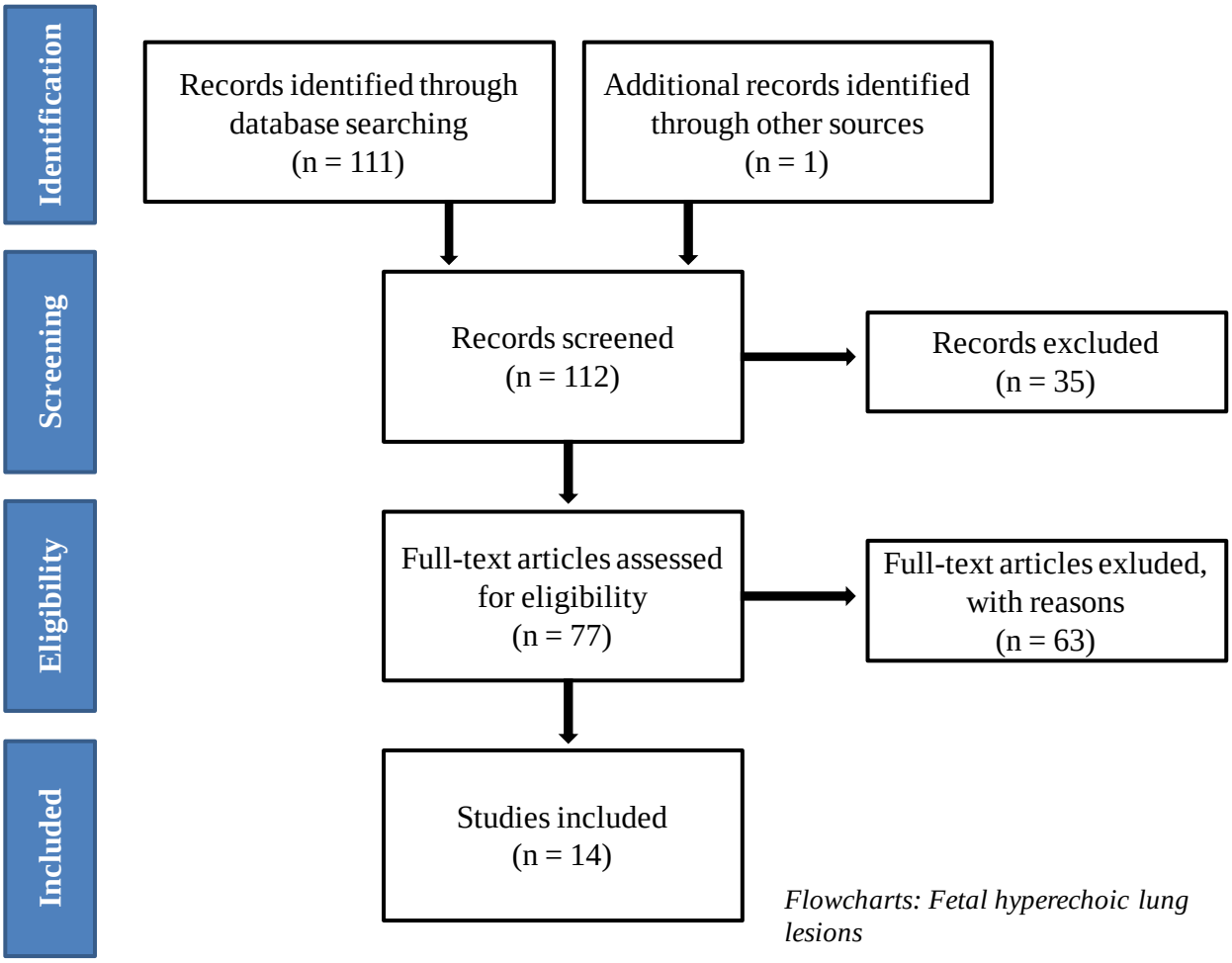
Flowcharts: Chorioangioma



Flowcharts: Sacrococcygeal teratoma



Flowcharts: Lower urinary tract obstruction



Flowcharts: Fetal hyperechoic lung lesions

PRENATAL DIAGNOSIS

ispd International Society for Prenatal Diagnosis

Review

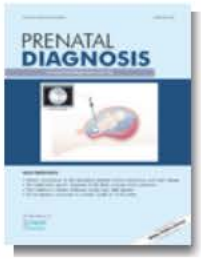
Fetal laser therapy: applications in the management of fetal pathologies

Jérôme Mathis, Luigi Raio and David Baud*

Article first published online: 5 APR 2015

DOI: 10.1002/pd.4587

Issue



Prenatal Diagnosis

Volume 35, Issue 7, pages 623–636, July 2015

Additional Information (Show All)

How to Cite | Author Information | Publication History

Funding sources: David Baud is supported by the 'Fondation Leenaards' through the 'Bourse pour la relève académique', the Divesa Foundation and the Swiss National Science Foundation (SNSF no. 310030-156169).

Conflicts of interest: None declared

Filename	Format	Size	Description
pd4587-sup-0001-Flowcharts.doc	Word document	79K	Supporting info item

Please note: Wiley Blackwell is not responsible for the content or functionality of any supporting information supplied by the authors. Any queries (other than missing content) should be directed to the corresponding author for the article.

View Full Article with Supporting Information (HTML) | Enhanced Article (HTML) | Get PDF (472K)

More content like this

Find more content: like this article

Find more content written by: Jérôme Mathis | Luigi Raio | David Baud | All Authors