Università degli Studi di Padova
Dipartimento di Salute della Donna e del Bambino – SDB
U.O.C. Clinica Ginecologica ed Ostetrica
Scuola di Specializzazione in Ginecologia e Ostetricia
Direttore Prof. Giovanni Battista Nardelli

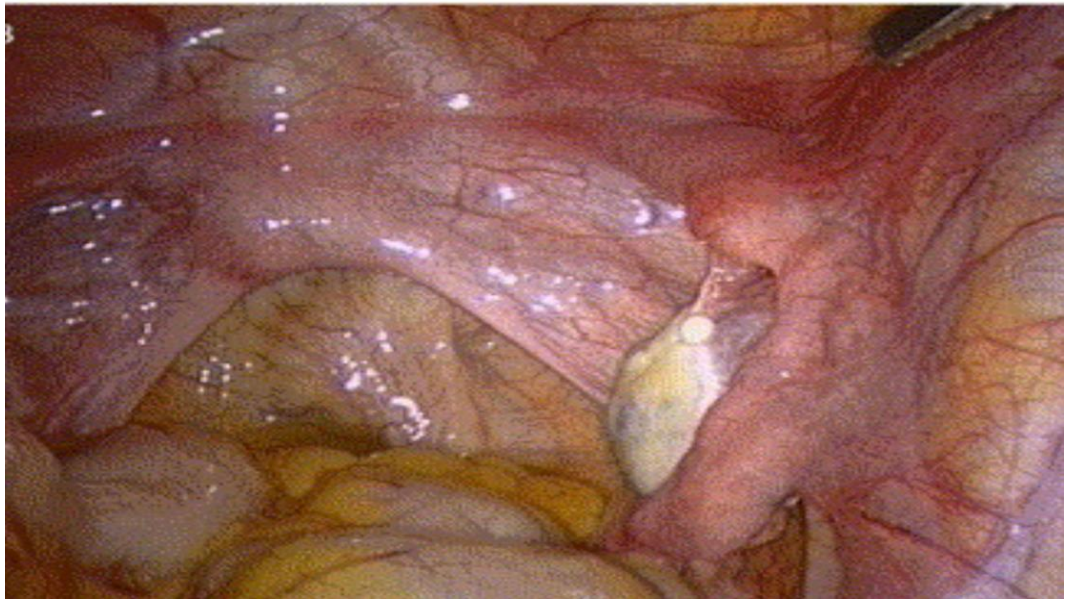
Malformazioni uterine: classificazione, diagnosi, trattamento ed outcome ostetrico

Dott.ssa L.Puma

Caso clinico 1

- Paziente di 41 aa PARA 0000
- An. Familiare: familiarità cardiomiopatia restrittiva
- An. fisiologica: Allergia allo iodio, diuresi regolare, alvo stiptico, nega tabagismo, nega E/P
- An. patologica remota: LPT 1984 appendicectomia LPT nel 1995: colecistectomia, ernioplastica inguinale destra, nefropessi. **Amenorrea primaria**
- An. Patologica prossima: **algie pelviche cicliche da 6 aa, associate a dorsalgie**
- RMN (09/06/2015): .. «**Utero ipoplasico, bicorne**, Vagina regolare, ovaie localizzate a ridosso della parete pelvica anteriore. A carico dell'ovaio estro si visualizza cisti di 26 mm a componente emorragica (cisti endometriosica?). Sottile free fluid pelvico».
- Esami ematochimici ed ECG preoperatori: nei limiti della norma
- **LPS diagnostica (11/11/2015):** « all'ispezione addomino pelvica si visualizzano due abbozzi di utero adesi alla parete laterale pelvica bilateralmente. Annesso destro regolare. A carico dell'ovaio sinistro si reperta follicolo di 2 cm. Tale quadro risulta riferibile a **Sndr. Mayer-Rokitansky-Kuster-Hauser**»

- **<u>LPS diagnostica (11/11/2015):</u>** « all'ispezione addomino pelvica si visualizzano due abbozzi di utero adesi alla parete laterale pelvica bilateralmente. Annesso destro regolare. A carico dell'ovaio sinistro si reperta follicolo di 2 cm. Tale quadro risulta riferibile a **Sndr. Mayer-Rokitansky-Kuster-Hauser**»



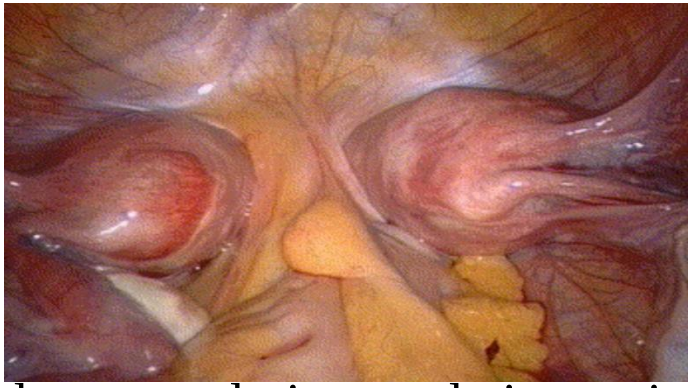
Caso clinico 2

- Paziente di 15 aa, PARA 0000, paziente virgo
- An. Familiare: ndp
- An fisiologica: nega allergie note, nega fumo, nega E/P, alvo e diuresi regolari, **cicli mestruali regolari**
- An patologica remota: **Monorene destro** noto dalla nascita, nega interventi chirurgici.
- An. Patologica prossima: 08/08/2015 **dolore addominale ingravescente da 7 gg**. Si reca al PS del P.O.S. di Milazzo.
- TAC addome senza MDC (08/08/2015): «Marcato aumento di dimensioni del terzo inferiore dell'utero, sostenuto dalla presenza di materiale end luminale a densità disomogenea. Non free fluid»
- RMN addome inferiore senza MDC (10/08/2015): «**Utero bicorne, bicolle, iperantiversoflesso con posizione alta delle due cervici**. La cervice destra si continua caudalmente con struttura tubulare(vagina destra??). La cervice sinistra si continua, caudalmente con voluminosa struttura a contenuto ematico (vagina sinistra con imene imperforato??) di 105x 52x48 mm, cranialmente risale lungo il retroperitoneo sino alla loggia renale sinistra (disabitata). Ovaie regolari per dimensioni e morfologia. Lievemente aumentate le dimensioni del rene destro»

LPS diagnostica + isteroscopia diagnostica fino ad operativa (09/10/2015):

- I tempo laparoscopico: Lisi di aderenze omentali colfondo uterino che presenta lieve deflessione in sede mediana.

  Annessi bilateralmente regolari.



- II tempo isteroscopico: in vagina

  si reperta orifizio uterino mediano destro;

  si esplorano il canale cervicale

- e l' emicavità uterina corrispondenti che risultano regolari con relativo ostio tubarico. Mediante Versapoint si amplia la cavità uterina. Si reperta inoltre un secondo orifizio uterino esterno mediano sinistro che risulta stenotico, in assenza di fornice vaginale. Si introduce l'isteroscopio repertando canale vaginale ed emicavità uterina normali con ostio tubarico regolare.si procede mediante Versapoint ad ampliare orifizio uterino esterno sinistro. La diagnosi posta è di **utero didelfo**.

Definizione

Anomalie anatomiche congenite risultanti dall'alterazione dei processi di formazione, fusione e riassorbimento dei dotti Mülleriani nel corso della vita fetale

- isolate/associate a malformazioni dell'apparato urinario (agenesia renale, ipoplasia renale, doppio uretere, uretere ectopico)
- possono alterare il potenziale riproduttivo delle pazienti o, nei casi più complessi, lo stato di salute

Epidemiologia

- Incidenza non è nota
- Prevalenza stimata nella popolazione generale: 2-3%
- Prevalenza variabile in letteratura dal 0.5%-5% fino al 38%
- Stima difficile

The prevalence of uterine anomalies in different study populations stratified by the accuracy of the diagnostic test used to identify and define them.

Population	Diagnostic test	Number of studies	Number of subjects	Prevalence of all anomalies % (95% CI)	Arcuate % (95% CI)	Canalization defects % (95% CI)	Unification defects			Others % (95% CI)
							Bicornuate % (95% CI)	Unicornuate % (95% CI)	Didelphys % (95% CI)	
Unselected	Optimal	9	5163	5.5 (3.5–8.5)	3.9 (2.1–7.1)	2.3 (1.8–2.9)	0.4 (0.2–0.6)	0.1 (0.1–0.3)	0.3 (0.1–0.6)	0.1 (0–2.2)
	Suboptimal	13	52 590	4.6 (2.3–9.1)	2.2 (0.9–5.2)	0.2 (0–0.9)	0.2 (0–0.7)	0.2 (0.1–0.5)	0.1 (0.1–0.2)	2.5 (1.6–3.7)
Infertility	Optimal	19	10 303	8.0 (5.3–12.0)	1.8 (0.8–4.1)	3.0 (1.3–6.7)	1.1 (0.6–2.0)*	0.5 (0.3–0.8)*	0.3 (0.2–0.5)	0.9 (0.4–1.8)
	Suboptimal	29	8643	6.1 (3.9–9.5)	5.8 (3.4–10.1)	2.7 (1.5–4.6)*	0.8 (0.5–1.4)	0.8 (0.5–1.2)	0.4 (0.2–0.9)	1.0 (0.4–2.4)
Miscarriage	Optimal	6	2082	13.3 (8.9–20)*	2.9 (0.9–9.6)	5.3 (1.7–16.8)*	2.1 (1.4–3)*	0.5 (0.3–1.1)*	0.6 (0.3–1.4)	0.9 (0.1–12.6)
	Suboptimal	21	3961	15.8 (11.9– 20.9)*	8.9 (6.4–12.4)*	4.3 (2.3–8.2)*	2.8 (1.6–5)*	0.5 (0.3–0.9)	0.6 (0.2–1.6)	4.5 (2–9.8)*
Mixed infertility and recurrent miscarriage	Optimal	9	7053	24.5 (18.3–32.8)*	6.6 (2.8–15.7)	15.4 (12.5–19)*	4.7 (2.9–7.6)*	3.1 (2–4.7)*	2.1 (1.4–3.2)*	0.3 (0–2.3)
	Suboptimal	1	66	31.8 (20.7–48.8)	No study found	None diagnosed	None diagnosed	4.5 (1.5–14.1)	None diagnosed	27.3 (17.2–43.3)*

No appropriate study investigating the prevalence of uterine anomalies in women with preterm deliveries was identified.

Optimal diagnostic tests: three-dimensional transvaginal ultrasound, laparoscopy or laparotomy with hysteroscopy or HSG, MRI, and saline sonohysterography.

Suboptimal diagnostic tests: two-dimensional transvaginal ultrasound, hysteroscopy, HSG and clinical assessment at the time of Caesarean section.

Studies with women undergoing IVF (three studies) were included in the infertile group.

* $P < 0.05$, differences are statistically significant when compared with an unselected population. Comparisons were made using meta-regression.

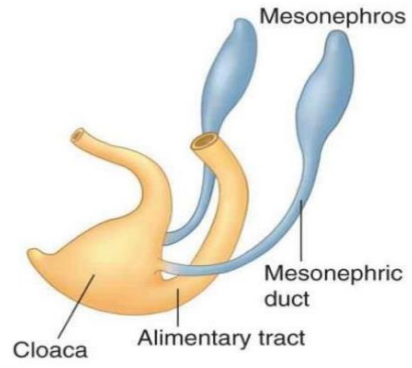
CI, confidence interval.

Fattori di rischio

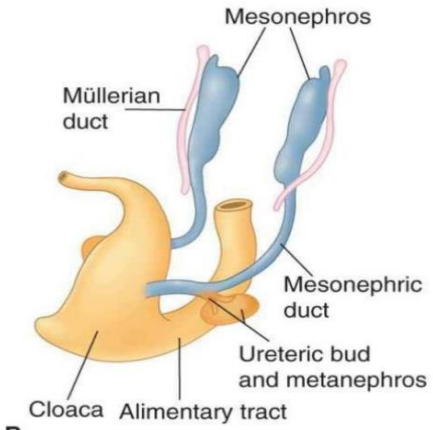
- Mutazioni a carico WNT/HOXA/LHX1/HNF1B (Sndr. Mayer-Rokitansky-Kuster-Hauser)

- Esposizione perinatale al DES

Embriologia



A



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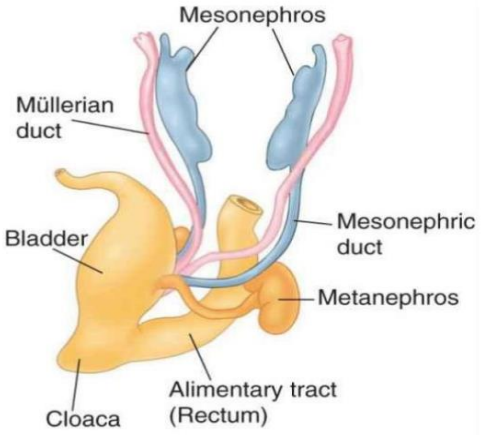
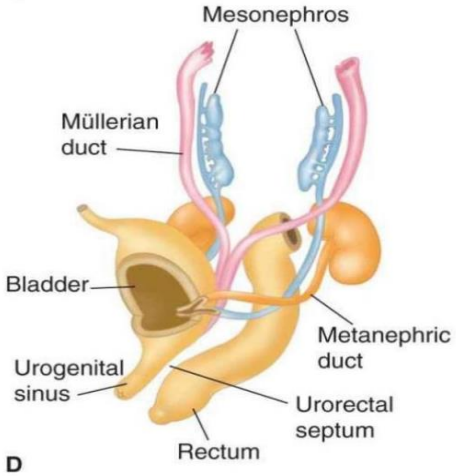


C



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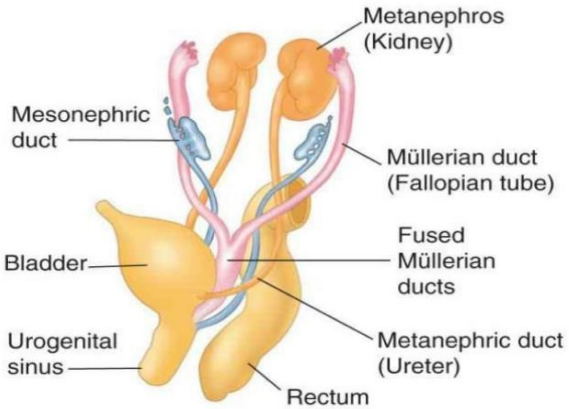

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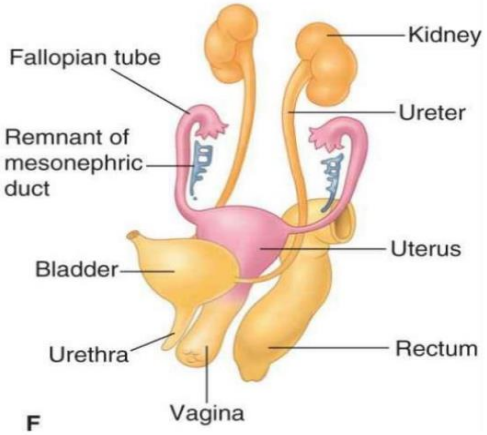
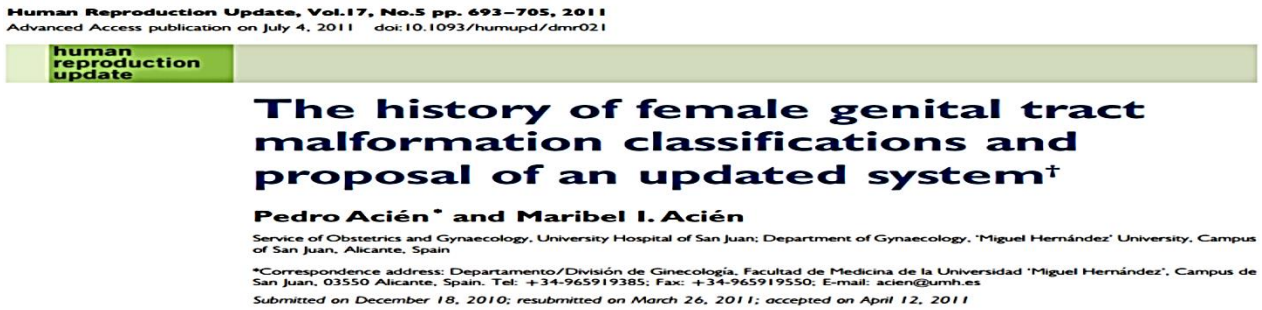


F

Errore nell'embriogenesi	Anomalia uterina
Fallimento nello sviluppo di uno o più dotti	Agenesia uterina Utero unicorne Utero unicorne con o senza corno rudimentario
Fallimento nella canalizzazione dei dotti	Utero unicorne con corno rudimentario senza cavità endometriale
Fallimento nella fusione dei dotti	Utero bicorne Utero didelfo
Fallimento nel riassorbimento	Utero setto completo Utero subsetto Utero arcuato

Classificazioni

- American Fertility Society 1988
- Acien et al. 2011



Human Reproduction Update, Vol.17, No.5 pp. 693–705, 2011
Advanced Access publication on July 4, 2011 doi:10.1093/humupd/dmr021

human reproduction update

The history of female genital tract malformation classifications and proposal of an updated system†

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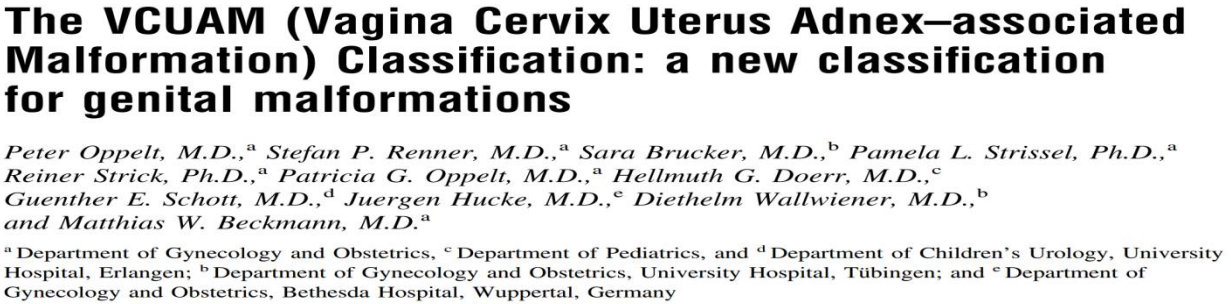
Submitted on December 18, 2010; resubmitted on March 26, 2011; accepted on April 12, 2011

- Oppelt P. et al. 2005

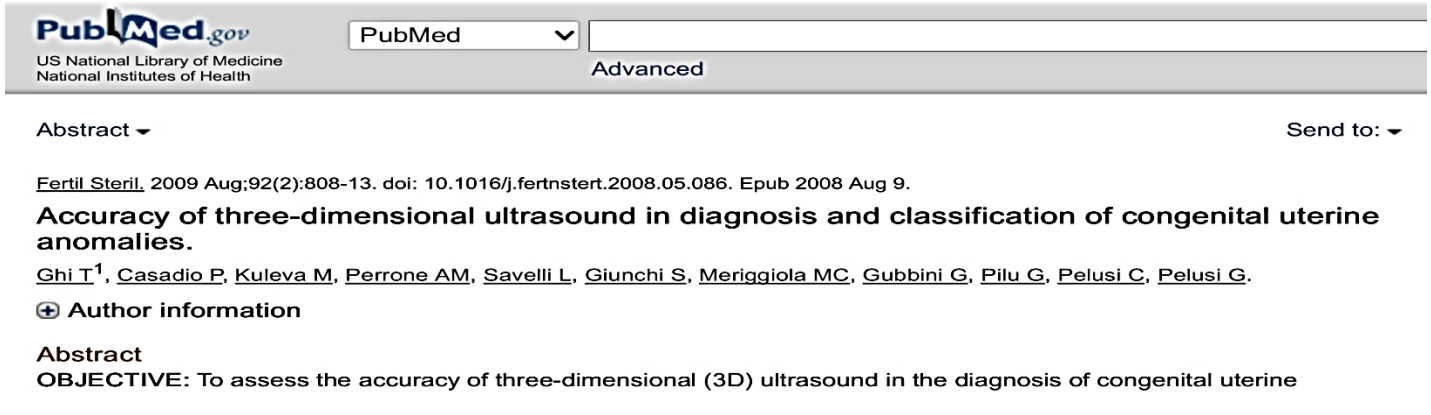


The VCUAM (Vagina Cervix Uterus Adnex–associated Malformation) Classification: a new classification for genital malformations

Peter Oppelt, M.D.,[a] Stefan P. Renner, M.D.,[a] Sara Brucker, M.D.,[b] Pamela L. Strissel, Ph.D.,[a] Reiner Strick, Ph.D.,[a] Patricia G. Oppelt, M.D.,[a] Hellmuth G. Doerr, M.D.,[c] Guenther E. Schott, M.D.,[d] Juergen Hucke, M.D.,[e] Diethelm Wallwiener, M.D.,[b] and Matthias W. Beckmann, M.D.[a]

[a] Department of Gynecology and Obstetrics, [c] Department of Pediatrics, and [d] Department of Children's Urology, University Hospital, Erlangen; [b] Department of Gynecology and Obstetrics, University Hospital, Tübingen; and [e] Department of Gynecology and Obstetrics, Bethesda Hospital, Wuppertal, Germany

- Ghi 2009



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Abstract

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Fertil Steril. 2009 Aug;92(2):808-13. doi: 10.1016/j.fertnstert.2008.05.086. Epub 2008 Aug 9.

Accuracy of three-dimensional ultrasound in diagnosis and classification of congenital uterine anomalies.

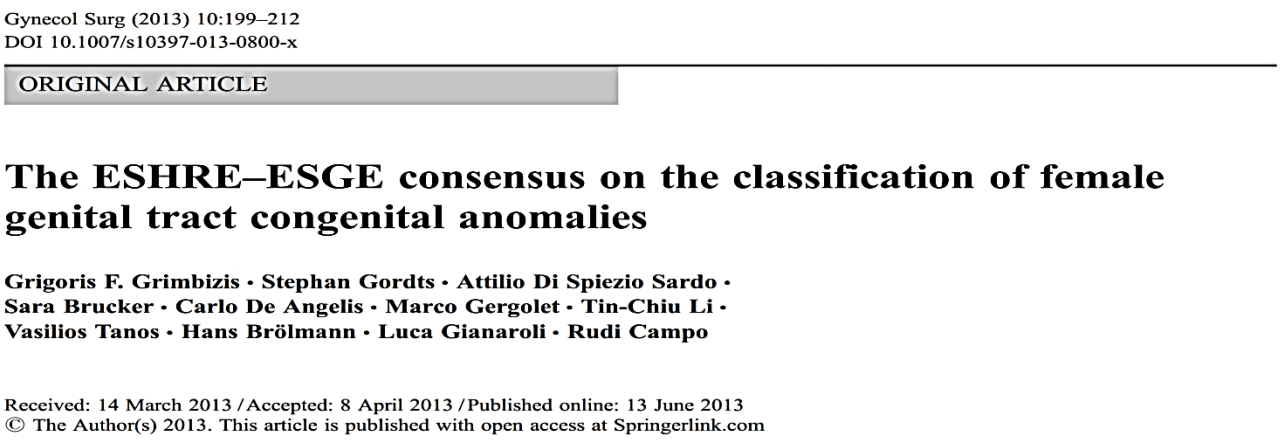
Ghi T[1], Casadio P, Kuleva M, Perrone AM, Savelli L, Giunchi S, Meriggiola MC, Gubbini G, Pilu G, Pelusi C, Pelusi G.

Author information

Abstract

OBJECTIVE: To assess the accuracy of three-dimensional (3D) ultrasound in the diagnosis of congenital uterine

- CONUTA 2013



Gynecol Surg (2013) 10:199–212
DOI 10.1007/s10397-013-0800-x

ORIGINAL ARTICLE

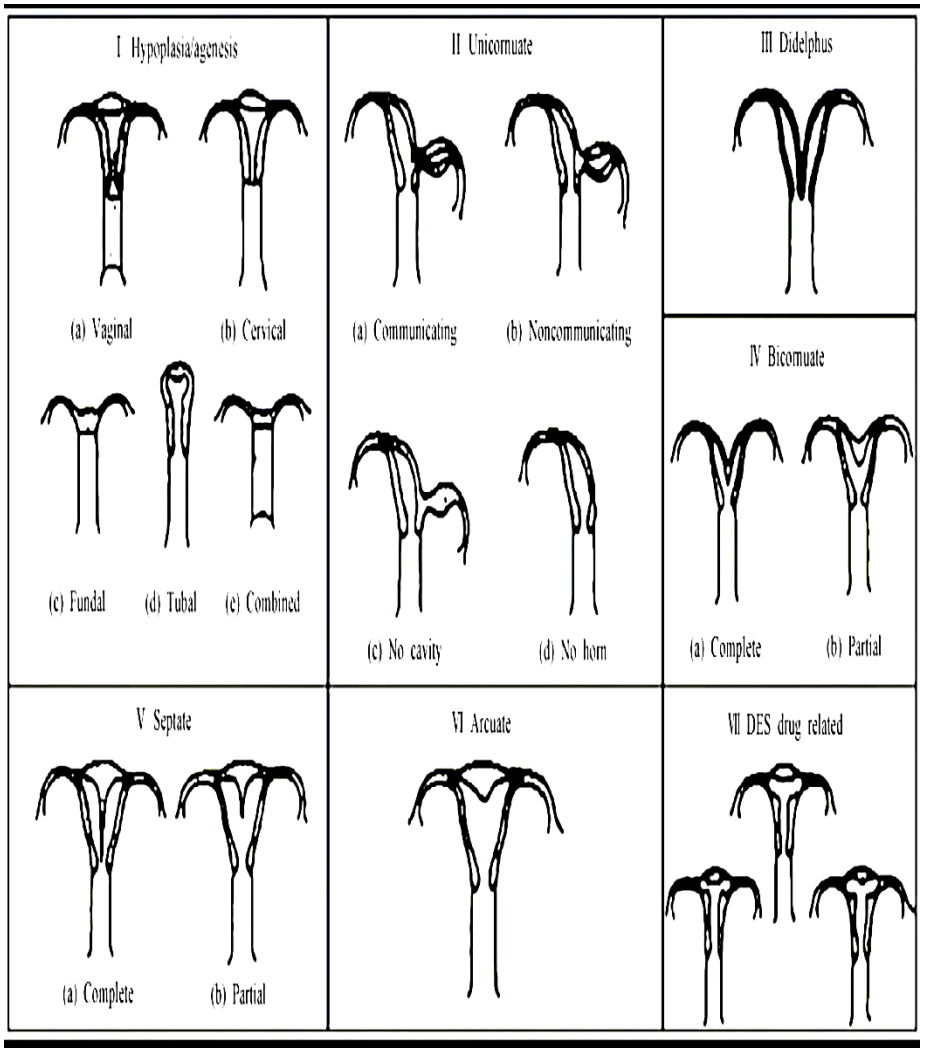
The ESHRE–ESGE consensus on the classification of female genital tract congenital anomalies

Grigoris F. Grimbizis · Stephan Gordts · Attilio Di Spiezio Sardo · Sara Brucker · Carlo De Angelis · Marco Gergolet · Tin-Chiu Li · Vasilios Tanos · Hans Brölmann · Luca Gianaroli · Rudi Campo

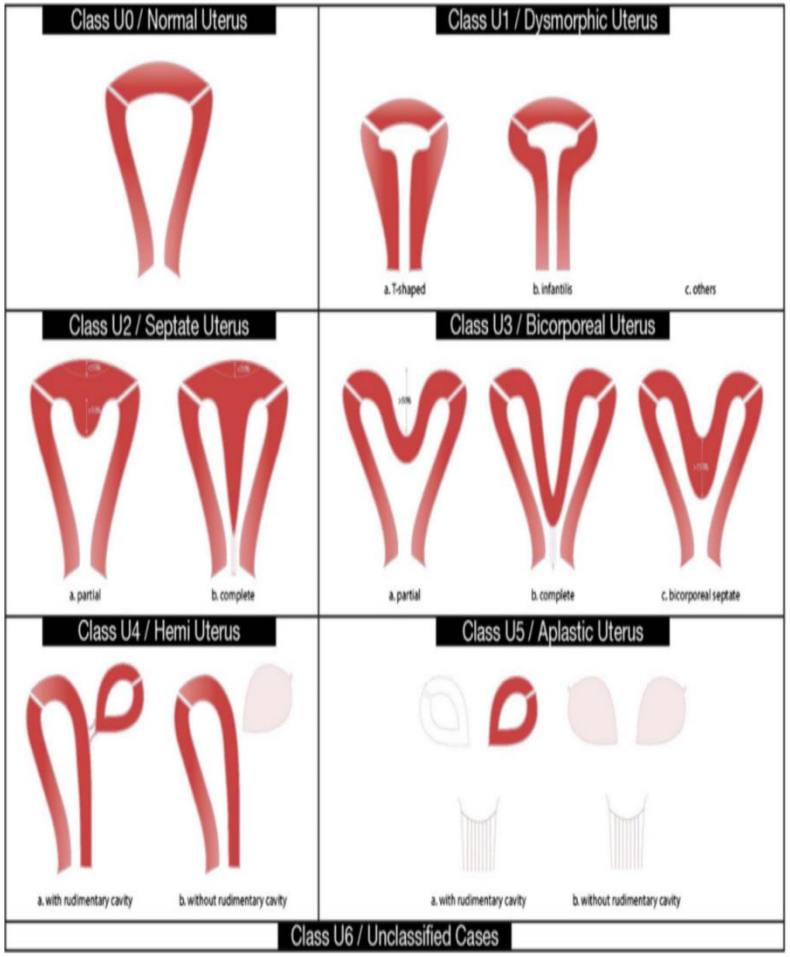
Received: 14 March 2013 / Accepted: 8 April 2013 / Published online: 13 June 2013

AFS 1988

- **I. Segmental müllerian hypoplasia or agenesis**
  - a. Vaginal
  - b. Cervical
  - c. Uterine
  - d. Tubal
  - e. Combined
- **II. Unicornuate uterus**
  - a. Rudimentary horn with cavity, communicating to unicornuate uterus
  - b. Rudimentary horn with cavity, not communicating to unicornuate uterus
  - c. Rudimentary horn with no cavity
  - d. Unicornuate uterus without a rudimentary horn
- **III. Uterine didelphys**
- **IV. Bicornuate uterus**
  - a. Complete bifurcation (bicollis)
  - b. Partial bifurcation (unicollis)
- **V. Septate uterus**
  - a. Complete septation
  - b. Partial septation
- **VI. Arcuate uterus**
- **VII. Diethylstilbestrol-related anomalies**



CONUTA 2013



	Uterine anomaly		Cervical / Vaginal anomaly	
	Main class	*Sub-class*	*Co-existent class*	
U0	Normal uterus		*C0*	*Normal cervix*
U1	Dysmorphic uterus	**a.** T-shaped **b.** Infantilis **c.** Others	*C1*	*Septate cervix*
U2	Septate uterus	**a.** Partial **b.** Complete	*C2*	*Double "normal" cervix*
U3	Bicorporeal uterus	**a.** Partial **b.** Complete **c.** Bicorporeal septate	*C3*	*Unilateral cervical aplasia*
U4	Hemi-uterus	**a.** With rudimentary cavity (communicating or not horn) **b.** Without rudimentary cavity (horn without cavity / no horn)	*C4*	*Cervical Aplasia*
U5	Aplastic	**a.** With rudimentary cavity (bi- or unilateral horn) **b.** Without rudimentary cavity (bi- or unilateral uterine remnants / Aplasia)	*V0*	*Normal vagina*
U6	Unclassified Malformations		*V1*	*Longitudinal non-obstructing vaginal septum*
			V2	*Longitudinal obstructing vaginal septum*
			V3	*Transverse vaginal septum and/or imperforate hymen*
			V4	*Vaginal aplasia*

Segni e sintomi

- Asintomatiche
- Amenorrea primaria con normale sviluppo dei caratteri secondari sessuali secondari
- Algie pelviche cicliche
- Anisomenorrea, spotting intermestruale
- Ematocolpo/ematometra
- Ritenzione urinaria acuta
- Stipsi prolungata
- Compressione vascolare (ridotto ritorno venoso)
- Endometriosi pelvica
- Outcome ostetrico sfavorevole

Quadri ostruttivi

Diagnosi

Indagini non invasive:

- Visita ginecologica
- Ecografia 2D TA/TV
- Ecografia 3D TA/TV
- Sonoisterosalpingografia
- RMN
- TAC

Indagini invasive:

- Isteroscopia
- Laparoscopia

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human reproduction ESHRE PAGES

The Thessaloniki ESHRE/ESGE consensus on diagnosis of female genital anomalies†

Grigoris F. Grimbizis*, Attilio Di Spiezio Sardo, Sotirios H. Saravelos, Stephan Gordts, Caterina Exacoustos, Dominique Van Schoubroeck, Carmina Bermejo, Nazar N. Amso, Geeta Nargund, Dirk Timmerman, Apostolos Athanasiadis, Sara Brucker, Carlo De Angelis, Marco Gergolet, Tin Chiu Li, Vasilios Tanos, Basil Tarlatzis, Roy Farquharson, Luca Gianaroli, and Rudi Campo

Congenital Uterine Anomalies (CONUTA) common ESHRE/ESGE Working Group and invited Experts, ESGE Central Office, Diestsevest 43/0001, 3000 Leuven, Belgium

*Correspondence address. 1st Department of Obstetrics & Gynecology, Aristotle University of Thessaloniki, Tsimiski 51 Street, 54623 Thessaloniki, Greece. E-mail: grigoris.grimbizis@gmail.com, grimbi@med.auth.gr

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Ultrasound Obstet Gynecol 2010; **35**: 593–601
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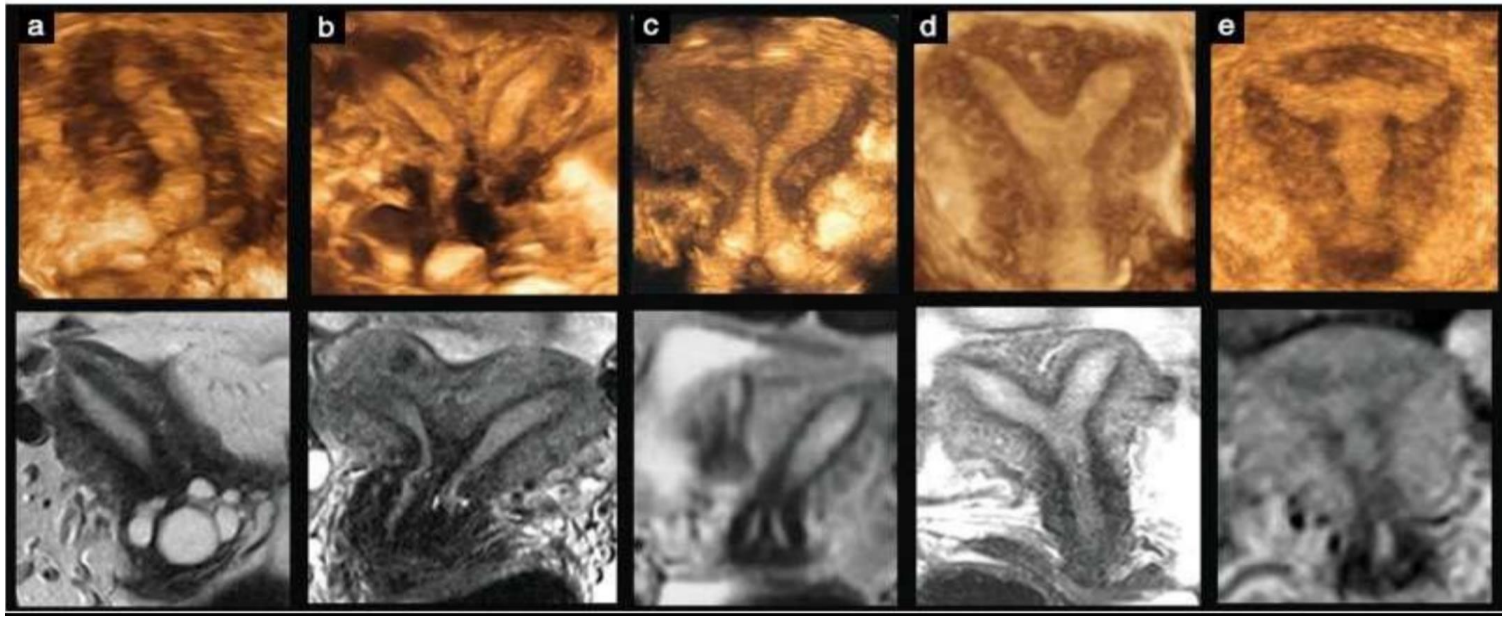
Three-dimensional ultrasound in the diagnosis of Müllerian duct anomalies and concordance with magnetic resonance imaging

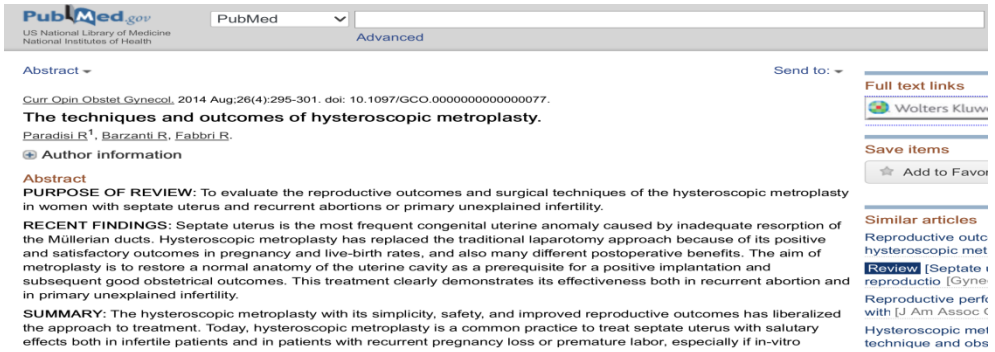
C. BERMEJO*, P. MARTÍNEZ TEN†, R. CANTARERO*, D. DIAZ*, J. PÉREZ PEDREGOSA‡, E. BARRÓN†, E. LABRADOR§ and L. RUIZ LÓPEZ¶

**Gabinete Médico Velazquez, †DELTA-Ultrasound Diagnostic Center in Obstetrics and Gynecology, ‡Department of Obstetrics and Gynecology, Hospital La Zarzuela and §Centro de Resonancia Magnética de Alto Campo Abirem, Madrid and ¶SESCAM, Spain*



Trattamento chirurgico

- Isteroscopico



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Curr Opin Obstet Gynecol. 2014 Aug;26(4):295-301. doi: 10.1097/GCO.0000000000000077.

The techniques and outcomes of hysteroscopic metroplasty.

Paradisi R[1], Barzanti R, Fabbri R.

Author information

Abstract

PURPOSE OF REVIEW: To evaluate the reproductive outcomes and surgical techniques of the hysteroscopic metroplasty in women with septate uterus and recurrent abortions or primary unexplained infertility.

RECENT FINDINGS: Septate uterus is the most frequent congenital uterine anomaly caused by inadequate resorption of the Müllerian ducts. Hysteroscopic metroplasty has replaced the traditional laparotomy approach because of its positive and satisfactory outcomes in pregnancy and live-birth rates, and also many different postoperative benefits. The aim of metroplasty is to restore a normal anatomy of the uterine cavity as a prerequisite for a positive implantation and subsequent good obstetrical outcomes. This treatment clearly demonstrates its effectiveness both in recurrent abortion and in primary unexplained infertility.

SUMMARY: The hysteroscopic metroplasty with its simplicity, safety, and improved reproductive outcomes has liberalized the approach to treatment. Today, hysteroscopic metroplasty is a common practice to treat septate uterus with salutary effects both in infertile patients and in patients with recurrent pregnancy loss or premature labor, especially if in-vitro

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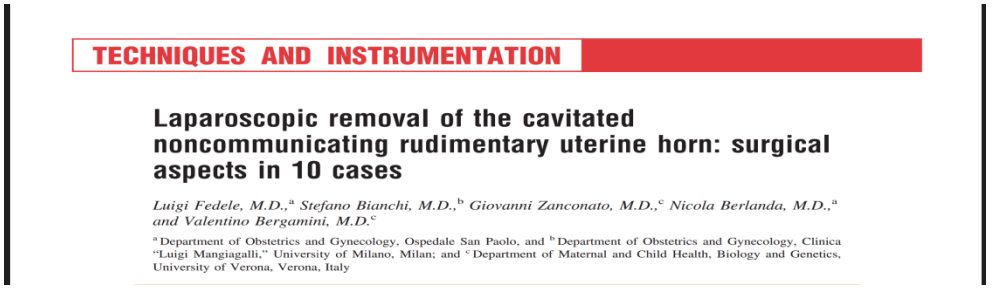


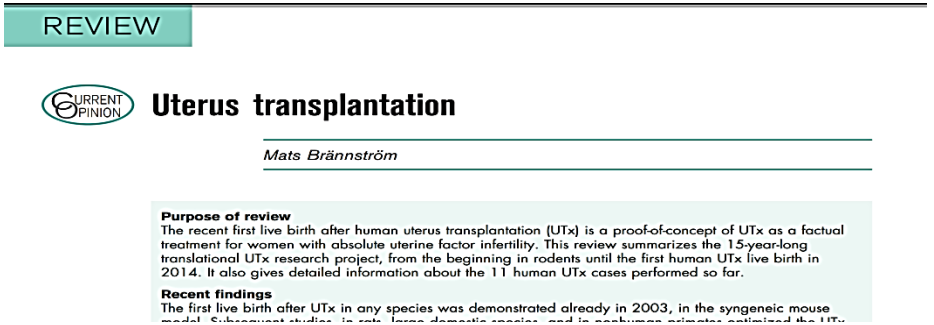
TECHNIQUES AND INSTRUMENTATION

Laparoscopic removal of the cavitated noncommunicating rudimentary uterine horn: surgical aspects in 10 cases

Luigi Fedele, M.D.,[a] Stefano Bianchi, M.D.,[b] Giovanni Zanconato, M.D.,[c] Nicola Berlanda, M.D.,[a] and Valentino Bergamini, M.D.[c]

[a] Department of Obstetrics and Gynecology, Ospedale San Paolo, and [b] Department of Obstetrics and Gynecology, Clinica "Luigi Mangiagalli," University of Milano, Milan; and [c] Department of Maternal and Child Health, Biology and Genetics, University of Verona, Verona, Italy

- Trapianto d'utero



REVIEW

CURRENT OPINION

Uterus transplantation

Mats Brännström

Purpose of review

The recent first live birth after human uterus transplantation (UTx) is a proof-of-concept of UTx as a factual treatment for women with absolute uterine factor infertility. This review summarizes the 15-year-long translational UTx research project, from the beginning in rodents until the first human UTx live birth in 2014. It also gives detailed information about the 11 human UTx cases performed so far.

Recent findings

The first live birth after UTx in any species was demonstrated already in 2003, in the syngeneic mouse

Outcome ostetrico

ELSEVIER

www.sciencedirect.com
www.rbmonline.com

Reproductive BioMedicine Online

REVIEW

Clinical implications of congenital uterine anomalies: a meta-analysis of comparative studies

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Table 2 Subgroup analysis according to the type of population analysed in each study.

	Non-specific population		*Infertile patients*		*Women who have experienced recurrent spontaneous abortions*		*Difference between subgroups*
	Studies	*RR (95% CI)*	*Studies*	*RR (95% CI)*	*Studies*	*RR (95% CI)*	*P*
Achievement of pregnancy	4	0.66 (0.37 to 1.19)	4	0.96 (0.89 to 1.04)	0	N/A	NS
Obstetric outcome							
First-trimester spontaneous abortion	5	1.88 (1.33 to 2.66)	3	1.24 (0.82 to 1.88)	1	1.07 (0.97 to 1.17)	0.006
Second-trimester spontaneous abortion	4	2.21 (1.40 to 3.48)	1	2.78 (0.83 to 9.32)	1	2.39 (1.32 to 4.33)	NS
First and second-trimester spontaneous abortion combined	6	2.28 (1.57 to 3.32)	5	1.46 (0.83 to 2.57)	3	1.13 (1.06 to 1.22)	0.001
Preterm delivery <37 weeks	8	2.25 (1.51 to 3.34)	1	2.49 (1.32 to 4.69)	1	1.73 (1.03 to 2.90)	NS
Preterm delivery <34 weeks	2	4.90 (3.52 to 6.84)	1	1.19 (0.32 to 4.48)	0	-	0.04
Preterm delivery <28 weeks	2	3.15 (0.94 to 10.54)	1	2.53 (0.58 to 11.02)	1	2.63 (1.04 to 6.62)	NS
Malpresentation at delivery	7	4.83 (3.20 to 7.29)	2	6.19 (0.91 to 42.05)	1	2.98 (1.20 to 7.38)	NS
Birth weight <2500 g	2	1.93 (1.50 to 2.49)	0	N/A	0	N/A	N/A
Birth weight <1500 g	2	2.07 (1.10 to 3.88)	0	N/A	0	N/A	N/A
Intrauterine growth restriction	2	3.17 (0.89 to 11.24)	0	N/A	0	N/A	N/A
Placental abruption	4	2.66 (1.36 to 5.23)	1	0.55 (0.03 to 11.34)	0	N/A	NS
Premature rupture of membranes	4	1.47 (0.69 to 3.15)	1	2.89 (1.01 to 8.31)	1	4.20 (0.47 to 37.24)	NS
Perinatal mortality	4	2.50 (1.33 to 4.69)	1	1.39 (0.13 to 15.09)	0	N/A	NS
The effect of hysteroscopic resection of the septum							
Achievement of pregnancy	1	0.96 (0.76 to 1.22)	1	2.16 (0.95 to 4.87)	2	1.09 (0.60 to 1.98)	NS
Spontaneous abortion	3	0.51 (0.27 to 1.00)	1	0.19 (0.06 to 0.56)	2	0.35 (0.20 to 0.61)	NS
Preterm labour <37 weeks	3	0.92 (0.27 to 3.14)	1	0.91 (0.14 to 5.85)	2	0.36 (0.09 to 1.42)	NS

N/A, not applicable; NS, not statistically significant.

Table 3 Pooled relative risks (95% confidence interval) for specific obstetric outcomes in women with congenital uterine anomolies compared with their controls.

	Arcuate	*Septated*	*Didelphys*	*Bicornuate*	*Unicornuate*	*Combined/undefined*
Preterm delivery <37 weeks	2.04 (0.99 to 4.19)	2.11 (1.51 to 2.94)	3.39 (2.06 to 5.58)	2.16 (1.55 to 3.02)	3.14 (1.90 to 5.18)	2.21 (1.59 to 3.08)
Premature delivery <34 weeks	1.19 (0.32 to 4.48)	N/A	N/A	N/A	N/A	3.81 (1.48 to 9.83)
Premature delivery <28 weeks	2.72 (0.53 to 14.06)	2.40 (0.46 to 12.42)	3.45 (0.40 to 29.83)	5.37 (1.53 to 18.80)	6.30 (0.29 to 137.42)	2.84 (1.52 to 5.31)
Malpresentation at delivery	2.53 (1.45 to 4.43)	4.35 (2.52 to 7.50)	2.62 (2.25 to 3.06)	4.65 (3.43 to 6.32)	3.12 (2.39 to 4.08)	4.75 (3.29 to 6.84)
Birth weight <2500 g	1.42 (0.74 to 2.72)	1.60 (0.94 to 2.71)	2.40 (1.40 to 4.11)	1.74 (1.13 to 2.69)	3.54 (2.22 to 5.64)	1.93 (1.50 to 2.49)
Birth weight <1500 g	1.95 (0.47 to 8.00)	1.97 (0.58 to 6.64)	1.15 (0.16 to 8.28)	2.78 (1.16 to 6.69)	3.18 (0.79 to 12.82)	2.07 (1.10 to 3.88)
Intrauterine growth restriction	5.03 (0.33 to 76.19)	2.54 (1.04 to 6.23)	4.94 (2.20 to 11.09)	2.80 (1.06 to 7.34)	3.54 (0.21 to 61.01)	3.17 (0.89 to 11.24)
Placental abruption	6.60 (2.35 to 18.53)	4.37 (1.12 to 17.08)	2.04 (0.28 to 15.10)	1.48 (0.29 to 7.55)	4.31 (0.77 to 23.97)	2.47 (1.28 to 4.77)
Premature rupture of membranes	1.67 (0.84 to 3.34)	0.61 (0.28 to 1.37)	1.30 (0.56 to 3.02)	1.12 (0.51 to 2.43)	0.54 (0.20 to 1.50)	1.74 (0.92 to 3.29)
Perinatal mortality	2.66 (0.89 to 7.93)	2.43 (1.10 to 5.36)	1.97 (0.69 to 5.66)	3.32 (1.61 to 6.86)	2.20 (0.76 to 6.39)	2.43 (1.34 to 4.42)