Cesarean Scar Pregnancy and Morbidly Adherent Placenta

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Disclosures

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Relevant Financial Relationships: None

Learning Objectives

After completing this presentation, the learner will be able to:

- Diagnose a cesarean scar pregnancy (CSP), by the diagnostic criteria and differentiate it from an intrauterine pregnancy (IUP) and a cervical pregnancy (CxP).
- Recognize that there is a common histologic basis of CSP and morbidly adherent placenta (MAP) such as accreta, increta and percreta, and that CSP is its main precursor and a major risk for MAP.
- Construct an evidence based counseling and management plan for the CSP considering the patients' obstetrical goals.
- Recognizing the sonographic findings of MAP.

Lecture Outline

1. What is a cesarean scar pregnancy
2. Pathogenesis
3. Incidence
4. Diagnosis and differential diagnoses
5. Natural history if left untreated
6. Treatment
   a. Choices in the literature
   b. Management complications
   c. Best treatment: Is there any single one?
7. Conclusions

1. What is a Cesarean Scar Pregnancy?

- Cesarean Scar Pregnancy (CSP) is a iatrogenic entity
- A blastocyst implants in a microscopic or macroscopic tract ***on*** the uterine scar or ***in*** the "niche" left by the incision, in the anterior uterine wall developing into a chorionic sac
- The mechanism is similar to implantations after uterine surgery (myomectomy, curettage, endometrial ablation, manual removal of placenta etc)

What is a CSP

- Clinically, CSP is a dangerous pregnancy presenting serious diagnostic, treatment and counseling challenges
- Synonyms in the literature: scar pregnancy, cesarean section scar ectopic, section scar ectopic
- Mistakenly considered an ectopic pregnancy (it IS low, but within the uterine cavity, left alone the sac "morphs " into the uterine cavity)
- Unless REAL ectopic pregnancies, it can result in a live neonate

What is a cesarean section scar/niche and how does it look?

On US, most of the time it appears like this:

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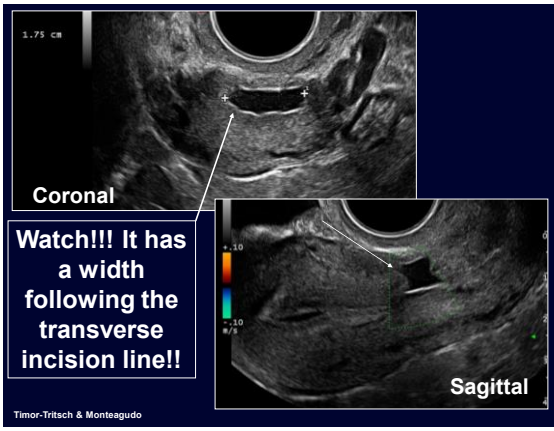

Watch!!! It has a width following the transverse incision line!!

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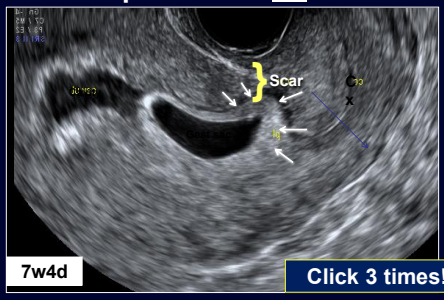
EARLY sonographic appearance:

Placenta implanted …"on the scar"…



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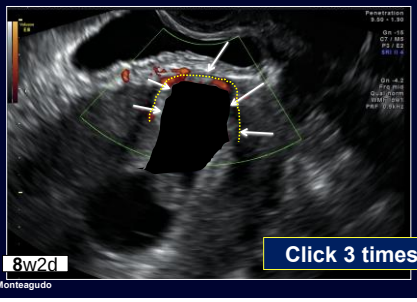
EARLY sonographic appearance:

Placenta implanted ….."in the niche"…



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2. Pathogenesis

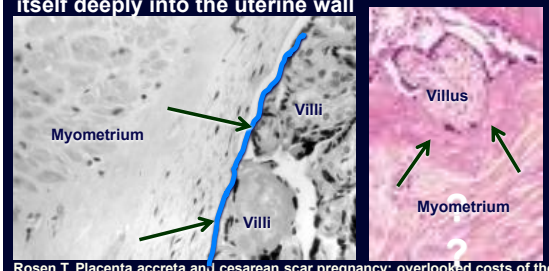
Theories of pathogenesis.

Previous uterine surgery or uterine interventions: lead to thin or absent decidua basalis in scarred areas of the lower uterine segment

Timor-Tritsch & Monteagudo . Clin Perinatol 2008;35:519-29,

Theories of the pathogenesis.

Uterine interventions lead to the thinning or missing Nitabuch fibrinoid layer. The placenta will attach itself deeply into the uterine wall



Rosen T. Placenta accreta and cesarean scar pregnancy: overlooked costs of the rising cesarean section rate. Clin Perinatol 2008;35:519-29,

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3. Incidence

- True incidence is not known
- ≈1 in 2000-2500 cesarean deliveries
- Rate closely related C/D rates
- 52% of CSPs had only one prior C/D
- The more previous C/D, the more CSP, the more placenta previa and accreta

Rotas MA et al, *Obstet Gynecol* 2006; 107: 1373-7.
Jurkovic D et al, *Obstet Gynecol* 2003; 21: 220-7.
Lin EP et al, RadioGraphics 2008; 28:1661–1671
Wu S et al, Am J Obstet Gynecol 2005;192:1458-61
Miller DA et al, Am J Obstet gynecol 1997; 177:210

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4. How do we make the diagnosis and which are the differential diagnoses?

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The sonograpic diagnosis is made reliably and in the Ob/Gyn office by transvaginal sonography

Diagnostic accuracy depends on the expertise and understanding its differential diagnostic issues

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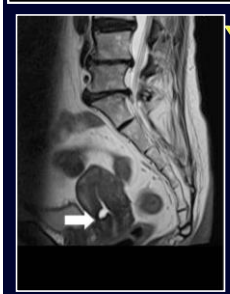
Should you order MRI to diagnose or to confirm a sono diagnosis of a CSP?



You could, but definitely not necessary! Why outsource, why delay diagnosis?

The first line imaging to diagnose or to confirm a CSP is transvaginal ultrasound!

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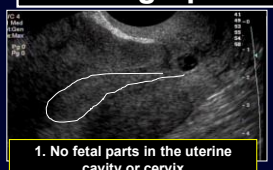
Sonographic criteria of CSP



1. No fetal parts in the uterine cavity or cervix

2. Thin myometrial layer between the bladder and & gestational sac

3. Triangular" shaped gestational sac*

4. Gestational sac close to the bladder and anterior uterine wall

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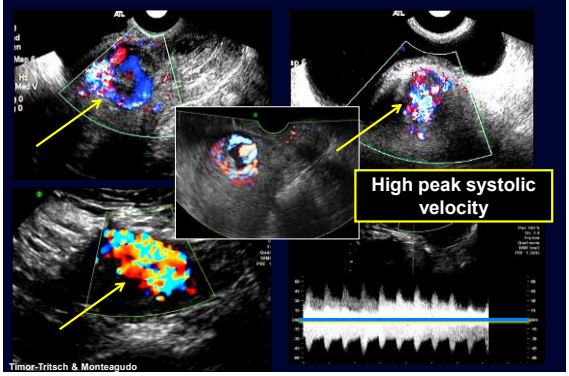
5. Rarely: A-V malformation at the site of a CS



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The differential diagnosis

1. **Cervical Pregnancy** – however – remember: Cx pregnancy is EXTREMELY rare & occur in intact uteri
2. **IUP** in the process of abortion – however – they very rarely have a beating heart!

Therefore:

If the chorionic sac is low, close to the cervix and the patient had a previous cesarean delivery: IT IS A CSP!!!!

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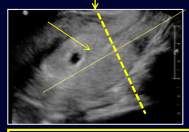
The easiest and simplest way to the diagnosis

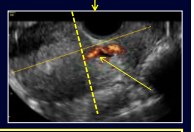
On a panoramic, longitudinal, sagittal scan determine the location of the gestational sac

↓

Divide the uterus in half by an imaginary line



Sensitivity = 93.0%,
Specificity = 98.9%,
+LR = 88.4%,
-LR = 0.07%.



If the gestational sac is above it: it is mostly a normal implantation

If the gestational sac is below it: suspect a CSP or a cervical pregnancy.

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Timor-Tritsch, ElRefaey, Monteagudo, Cali: AJOG 2016

Warning:
At times (mostly after 7 weeks) the location of the sac of a CSP may be misleading.

Rely on the patient's Hx, location of the placenta and its vascular supply!

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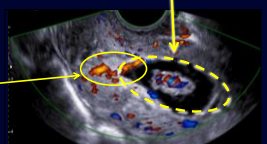
After 7 -8 weeks don't be "fooled" by the location of the sac!

In an anteverted uterus 7w2d

The sac may "move up", but the placenta with its vessels stays at implantation site

Rely on color Doppler of the vessels at the scar implantation site. They stay anchored!



In a retroverted uterus 9w2d

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Don't promiss your patient that it may not re-occur

- Recurrent CSP in the literature: ≈2%
  - 9/751 cases in one review: 1.2%^
    - 8 women had recurrent scar pregnancy*
    - 1 molar pregnancy in t1 he scar**
  - 1 had 5 consecutive CSPs!***
  - 21/619 cases in another review: 3.4% ****

* Hasegawa UOG 2005, Mabuchi Obster Gynecol Survey 2009, Holland Obst Gyneco 2008 (x2), Ben Nagi UOG 2007, Timor Tritsch UOG 2011. ** Wu CJ 2006. *** Gupta S, Timor-Tritsch I AJOG 2013. ****Zhi-Da Quian et al Fert Steil 2013

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5. What is the natural history of CSP?

First let us answer this question:

a. **Are CSP and MAP the same disease?**

If they are the same disease, they have to share the same histology

"Cesarean scar pregnancy and early placenta accreta (EPA) share a common histology"

- **Objective:** We evaluated the histology CSP & EPA in the second trimester
- Our hypothesis was: they are pathologically indistinguishable diseases; and represent an early clinical manifestation in the **continuum of morbidly adherent placenta.**

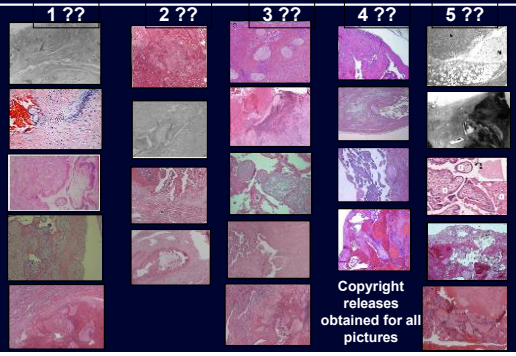
Timor-Tritsch IE, Monteagudo A, Cali G, Palacios-Jaraquemada JM, Maymon R, Arslan AA, Patil N, Popiolek D, Mittal KR.Ultrasound Obstet Gynecol. 2013

Materials and Methods:

- We reviewed 30 articles with 31 cases of CSP &13 cases of EPA
- We added 3 CSP and 7 EPA cases
- Two pathologists examined all the material separately and blinded to each other providing pathological diagnosis based on their microscopic appearance.
- Inter-observer correlation between them determined

Histologic specimens courtesy of Drs: J.P. Jaraquemada (Argentina), P. Cali (Italy) , R. Maymon (Israel) and A. Rygh (Norway) and J. Einenkel E (Germany)

2 Pathologists independently and blinded to clinical data examined the microscopic CSP and MAP slides



Evaluation of the pathologic slides

- All revealed placental villi invading the myometrium without an intervening decidua.
- It was impossible to determine the clinical diagnosis based upon the histologic picture.
- They were all consistent with adherent placentae of different degrees (placenta accreta, increta or percreta).

Timor-Tritsch IE, Monteagudo A, Cali G, Palacios-Jaraquemada JM, Maymon R, Arslan AA, Patil N, Popiolek D, Mittal KR.Ultrasound Obstet Gynecol. 2013

Conclusions:

- This study supports our hypothesis, that Cesarean Scar Pregnancy and Early Placenta Accreta are one and the same histopathologic entity and CSP is an early manifestation of morbidly adherent placenta.

Timor-Tritsch IE, Monteagudo A, Cali G, Palacios-Jaraquemada JM, Maymon R, Arslan AA, Patil N, Popiolek D, Mittal KR.Ultrasound Obstet Gynecol. 2013

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Placenta accreta and percreta can occur in the 1st trimester

- Fact based upon:
- Reports of massive hemorrhage during D&C and histology of MAP in the involved uteri*
- Reports of proven 1st Δ US and subsequent histology of MAP in the near term placenta
  - In all 6 of the cases of Comstock** and 10 cases of Ballas*** previous C/D was the risk factor

* Wolcot RJ et al 1987; Ecker JL et al 1992; Walter AJ et al 1999; Gherman RB et al 1999
** Comstock CH et al . JUM 2003
*** Ballas J et al . JUM 2012

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The antenatal diagnosis of placenta accreta

CH Comstock,[a,b,c] RA Bronsteen[a]

[a] Department of Obstetrics and Gynecology, William Beaumont Hospital, Royal Oak, MI, USA [b] Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, MI, USA [c] Department of Obstetrics and Gynecology, Wayne State University, Detroit, MI, USA
Correspondence: CH Comstock, William Beaumont Hospital, Division of Fetal Imaging, 3601 West Thirteen Mile Road, Royal Oak, MI 48071, USA. Email chcomstock@comcast.net

In the first trimester…..

Comstock CH, Bronsteen RA. The antenatal diagnosis of placenta accreta. BJOG 2014;121:171–182.

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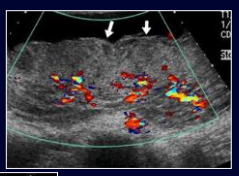

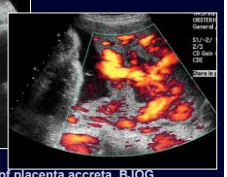

Comstock CH, Bronsteen RA. The antenatal diagnosis of placenta accreta. BJOG 2014;121:171–182.

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Additional literature support for the fact that CSP is one of the precursors of placenta accreta

Identifying Sonographic Markers for Placenta Accreta in the First Trimester

Jeranimos Ballas, MD, MPH, Dolores Pretorius, MD, Andrew Gladys A. Ramos, MD

J Ultrasound Med 2012; 31:1835–1841

Outcome of Cesarean Scar Pregnancies Diagnosed Sonographically in the First Trimester

J Ultrasound Med. 2015 Apr;34(4):595-9. d

Aya Y. Michaels, MD, Erin E. Washburn, MD, Katherine D. Pocius, MD, Carol B. Benson, MD, Peter M. Doubilet, MD, PhD, Daniela A. Carusi, MD

Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.14775

Natural history of early first-trimester pregnancies implanted in Cesarean scars

N. ZOSMER*, J. FULLER*, H. SHAIKH†, J. JOHNS* and J. A. ROSS*

*Early Pregnancy Unit, Kings College Hospital, London, UK; †Department of Histopathology, Kings College Hospital, London, UK

Sonographic Findings of Morbidly Adherent Placenta in the First Trimester

J Ultrasound Med 2016; 35:263–269 |

Martha W. F. Rac, MD, Elysia Moschos, MD, C. Edward Wells, MD, Donald D. McIntire, PhD, Jodi S. Dashe, MD, Diane M. Twickler, MD

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5. What is the natural history of CSP?

Let us answer the second question:

b. Is CSP a precursor of MAP?

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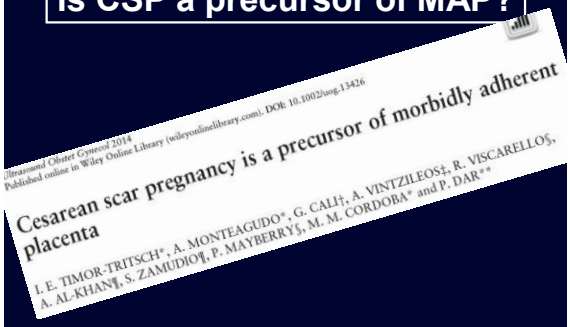
Is CSP a precursor of MAP?



Cesarean scar pregnancy is a precursor of morbidly adherent placenta

I. E. TIMOR-TRITSCH*, A. MONTEAGUDO*, G. CALI†, A. VINTZILEOS‡, R. VISCARELLO§, A. AL-KHAN¶, S. ZAMUDIO¶, P. MAYBERRY§, M. M. CORDOBA* and P. DAR**

Ultrasound Obstet Gynecol 2014; Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.13426

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CSP is a precursor of MAP

- The cases in the literature validate the fact that CSP is a precursor of MAP
- Pregnancies that start out as CSP may achieve birth of a live neonate.
- Case series present evidence upon which to counsel patients with CSP, enableing them to make an informed choice between 1stΔ TOP and continuation of the pregnancy, risk in premature delivery, hysterectomy, loosing fertility.

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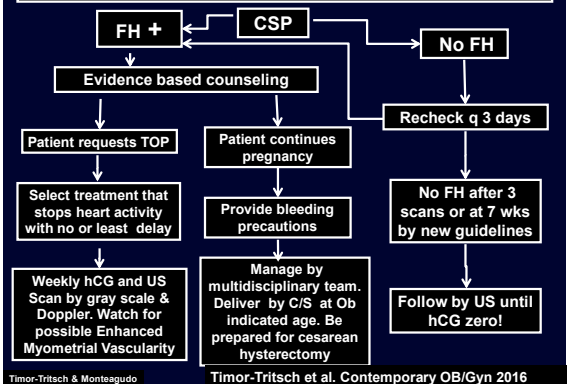
Suggested management of CSP



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Timor-Tritsch et al. Contemporary OB/Gyn 2016

6. First trimester treatment choices, if continuing the pregnancy is NOT an option

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Treatment

1. Choices in the literature
2. Management complications
3. Best treatment: Is there any single one?

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The major treatment modalities

- Surgical requiring general anesthesia
  - Major: laparotomy
  - Minor: Laparoscopy, Hysteroscopy; D&C
- Minimally invasive: Local injection (MTX/KCl)
- Systemic
  - Major: UAE
  - Minor: IM Methotrexate (single/multiple
- Different combinations of the above
  - Simultaneously
  - Sequentially

·Timor-Tritsch IE, Monteagudo A. Unforeseen consequences of the increasing rate of cesarean deliveries: early placenta accreta and cesarean scar pregnancy. A review. Am J Obstet Gynecol. 2012 Jul;207(1):14-29

·Birch Petersen K, Hoffmann E, Rifbjerg Larsen C, Nielsen HS. Cesarean scar pregnancy: a systematic review of treatment studies. Fertil Steril. 2016 Jan 18..[Epub ahead of print]

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Primary treatment in 751 cases

1. Hysreroscopic excision
2. Hysteroscopy by TAS guidance
3. Hysteroscopy & Mefipristone
4. Laparotomy & excision
5. Laparotomy with elective TAH
6. Laparotomy & systemic MTX
7. Laparotomy & hysteroscopy
8. TAS guided local MTX injection
9. TAS guided local KCl injection
10. TAS guided local & systemic MTX
11. TVS guided local MTX injection
12. TVS guided local KCl injection
13. TVS guided local & systemic MTX
14. Local injection of Vasopressin
15. 15. UA embolization alone
16. UA embolization & systemic MTX
17. UA embolization & local MTX
18. D&C alone
19. D&C & systemic MTX
20. D&C & Shirodkar cervical suture
21. Laparoscopic excision
22. Laparoscopy & hysteroscopy
23. Laparoscopy & systemic MTX
24. MTX systemic alone
25. MTX systemic & hysteroscopy
26. Expectant management
27. Trichostatin
28. Transrectal US guided aspiration
29. Hysteroscopy & Vasopressin
30. Hysterectomy by vaginal approach
31. Combination of ≥3 Rx. Modalities

After 2012 an additional 5-6 treatments were published

Timor-Tritsch 2012 AJOG

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Treatment

1. Choices in the literature
2. **Management complications**
3. Best treatment: Is there any single one?

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Treatment complications

Before treating: know the complications!

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Complication rate

- **Definition of "complication":**
- Immediate or delayed need for a 2ry treatment involving: blood loss > 200 ml, blood transfusion, general anesthesia, surgical approach/es
- The above were applied alone or in combination

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Timor-Tritsch IE, Monteagudo A. Unforeseen consequences of the increasing rate of cesarean deliveries: early placenta accreta and cesarean scar pregnancy. A review. Am J Obstet Gynecol. 2012;207(1):14-29

Complication rate in 751 cases

Overall: 331 (44.1%)

Timor-Tritsch IE, Monteagudo A. Unforeseen consequences of the increasing rate of cesarean deliveries: early placenta accreta and cesarean scar pregnancy. A review. Am J Obstet Gynecol. 2012;207(1):14-29

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Most and least complications by mode of treatment

Most frequently used single & combination Rx	# of cases	# of complications	%
MTX alone	87	54	62.1
D& C	305	189	61.9
UA embolization	64	30	46.9
Hysteroscopy	119	22	18.4
Local injection of MTX/KCl (TAS or TVS guidance)	81	8	9.6

Timor-Tritsch IE, Monteagudo A. Unforeseen consequences of the increasing rate of cesarean deliveries: early placenta accreta and cesarean scar pregnancy. A review. Am J Obstet Gynecol. 2012;207(1):14-29

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1. Treatment
   1. Choices in the literature
   2. Management complications
   3. **Best treatment: Is there any single one?**

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Which treatment to use??

The sporadic, mostly individual cases, case series and their results were insufficient to enable a clear conclusion as to which was the most effective, least invasive management protocol leading to the minimal or no complications.

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Are there guidelines??

In 2016: none of the countries, USA included, have a set of guidelines at hand when a patient with an early,1st trimester placenta accreta or a cesarean scar pregncy presents.

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Analysis of the most frequently used treatments based upon a review of 751 cases and case series published until 2012

Timor-Tritsch IE, Monteagudo A. Unforeseen consequences of the increasing rate of cesarean deliveries: early placenta accreta & cesarean scar pregnancy. A review. Am J Obstet Gynecol; 2012; 207:14

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Systemic MTX alone

- As a single agent treatment had a 64.6% complication rate.
- Its slow action may take days
- Questionable ability to stop the heart Often require additional treatment.

Sequential, multidose systemic MTX

- Be aware of its side effects.
- Even such treatment fails at times
- However MTX can be used as an adjuvant therapy with other treatments

Timor-Tritsch IE, Monteagudo A. Unforeseen consequences of the increasing rate of cesarean deliveries: early placenta accreta and cesarean scar pregnancy. A review. AJOG 2012;207(1):14-29

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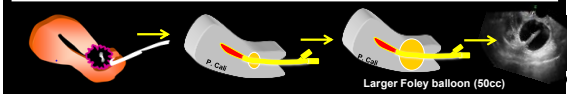
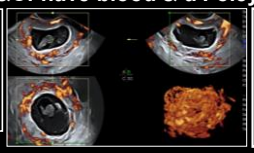
Suction aspiration and/or SHARP D&C alone or in combined with inflation of Foley balloon



Larger Foley balloon (50cc)

About 305 D&C cases reviewed in the literature with about 62% (29-86%) mostly bleeding complications
If planning D&C: have blood & a Foley balloon handy

3D US display of rich vascular supply surrounding the chorionic sac of a scar pregnancy



This explains the possible bleeding complication of a D&C when the scar pregnancy is subjected to curettage

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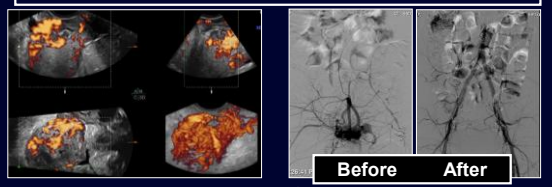
Uterine Artery Embolization alone or in combination wit other treatments



As single treatment has 47% complications/ failure*
Not the best"single"or "first line" treatment**
Adequate adjuvant to other treatments.
Uterus saving solution

*Vilos AG et al. Uterine artery embolization for uterine arteriovenous malformation in five women desiring fertility: pregnancy outcomes. Hum Reprod. 2015;30(7):1599-605
** Timor-Tritsch IE et al. Unforeseen consequences of the increasing rate of cesarean deliveries: early placenta accreta and cesarean scar pregnancy. A review. AJOG. 2012 ;207:14-29.

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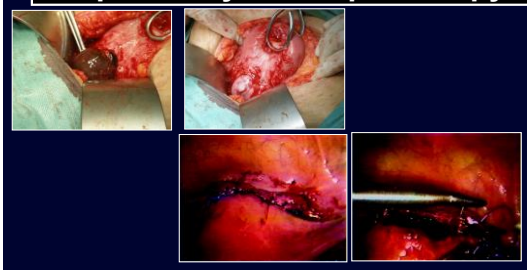
Laparotomy and Laparoscopy



14 cases reviewed in the literature with about 28% complications unless it results in TAH
(Complications were: infection, bleeding, anesthesia)

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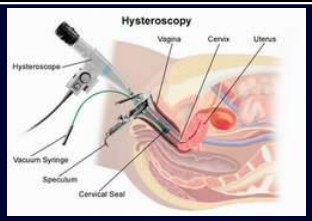
Timor-Tritsch 2012 AJOG

Operative hysteroscopy alone or in combination



About 119 cases reviewed in the literature with the second lowest (about 18%) complication rate (mostly bleeding)

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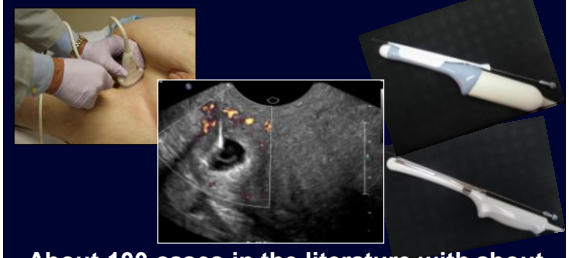
Timor-Tritsch 2012 AJOG

Transabdominal or transvaginal US guided local, intra-gestational sac injection of MTX/ KCl



About 100 cases in the literature with about an 9.6% (0-15%) complications

Michaels et al JUM 2015; Timor-Tritsch et al 2015; Zosmer et al UOG 2015

Timor-Tritsch & Monteagudo

Outcome of Cesarean Scar Pregnancies Diagnosed Sonographically in the First Trimester

J Ultrasound Med 2015; 34:595–599

Aya Y. Michaels, MD, Erin E. Washburn, MD, Katherine D. Pocius, MD, Carol B. Benson, MD, Peter M. Doubilet, MD, PhD, Daniela A. Carusi, MD

Cesarean Scar Pregnancies

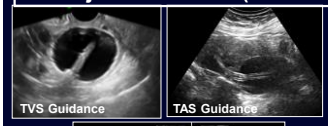
Experience of 60 Cases

J Ultrasound Med 2015; 34:601–610

Ilan E. Timor-Tritsch, MD, Nizar Khatib, MD, Ana Monteagudo, MD, Joanne Ramos, RDMS, Robert Berg, MD, Sándor Kovács, MD

Timor-Tritsch & Monteagudo

Transabdominal or transvaginal US guided Foley balloon placement to prevent bleeding after local injection of CSP (and cervical pregnancy)



Use as an adjuvant to:

- Local injection
- Aspiration or D&C
- Hysteroscopic excision
- Uterine Artery Embolization
- Laparoscopic excision

Ultrasound Obstet Gynecol 2015; 46: 118–121
Published online 8 June 2015 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.14708

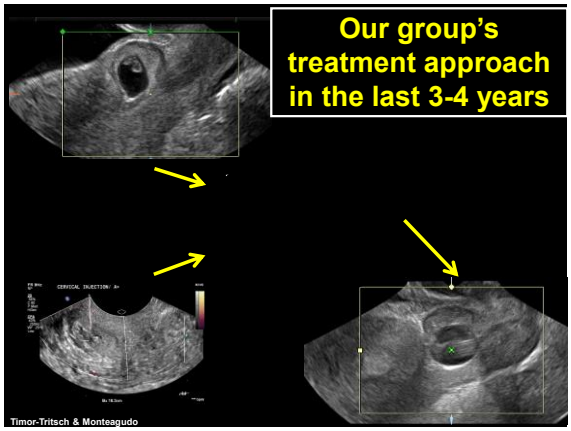
Foley balloon catheter to prevent or manage bleeding during treatment for cervical and Cesarean scar pregnancy

I. E. TIMOR-TRITSCH*, G. CALI†, A. MONTEAGUDO*, N. KHATIB‡, R. E. BERG*, F. FORLANI† and E. AVIZOVA*

Timor-Tritsch & Monteagudo

The use of a single balloon Foley catheter as andjuvant to local, intragestational injection of MTX

Timor-Tritsch & Monteagudo



Timor-Tritsch & Monteagudo

The use of a double, cervical ripening balloon catheter as a single, minimally invasive treatment

Timor-Tritsch & Monteagudo

Lately: New, minimally invasive treatment: Placing a double cervical ripening balloon

Reasons for its use:

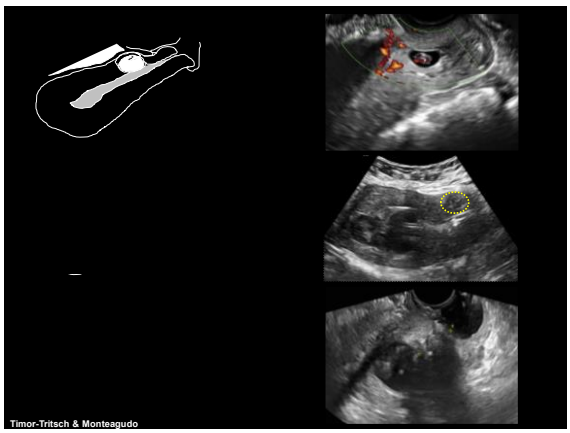
- Simultaneously terminates pregnancy and prevents bleeding
- Simplify treatment; Minimize patient discomfort
- Adapt a catheter familiar to Ob in the L&D to treat CSP
- Also effective for cervical pregnancies

The double balloon catheter

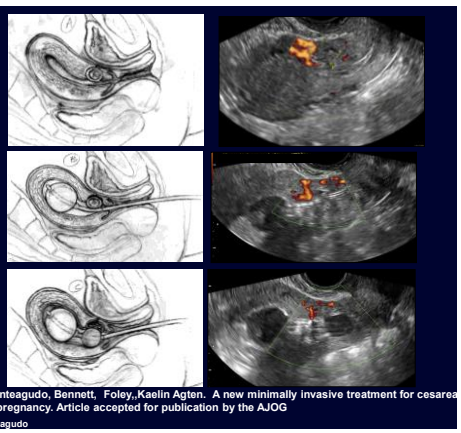
The balloons inflated

Timor-Tritsch, Monteagudo, Bennett, Foley, Kaelin Agten. A new minimally invasive treatment for cesarean scar and cervical pregnancy. Article accepted for publication by AJOG

Timor-Tritsch & Monteagudo

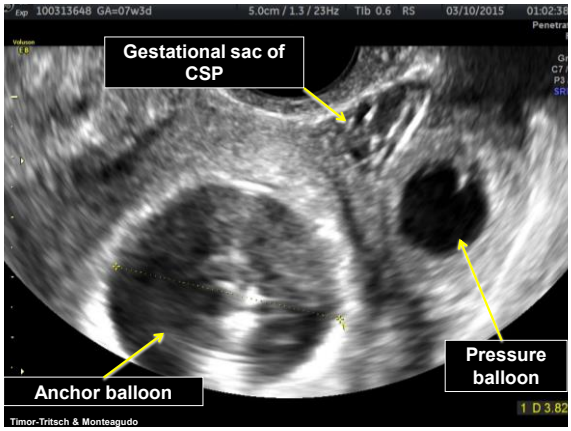


Timor-Tritsch & Monteagudo



Timor-Tritsch, Monteagudo, Bennett, Foley,, Kaelin Agten. A new minimally invasive treatment for cesarea scar and cervical pregnancy. Article accepted for publication by the AJOG

Timor-Tritsch & Monteagudo



Timor-Tritsch & Monteagudo

Our experience*

- 17 CSPs and 3 CxPs were treated.
- Patients tolerated balloon placement and inflation well
- Oral pain medication and antibiotics were given
- The last 6 patient in the series received paracervical block using 1% Lidocaine
- Minimal, "old", dark blood was seen after removal of the catheters probably from intracavitary accumulation of blood
- In all cases almost total resolution of the hCG, the sac site & its vascularity was seen within 50 -80 days

* Ending June 2016

Timor-Tritsch, Monteagudo, Bennett, Foley,,Kaelin Agten. A new minimally invasive treatment for cesarean scar and cervical pregnancy. AJOG 2016 Accepted article

Timor-Tritsch & Monteagudo

Cesarean scar pregnancy: a systematic review of treatment studies.

- **OBJECTIVE:** To study treatment modalities for cesarean scar pregnancies (CSPs), focusing on efficacy & complications relative to study quality.
- DESIGN: Systematic review.
- PATIENT(S): A total of 2,037 women with CSP.
- MAIN OUTCOME MEASURE(S): Successful 1st-line treatment. Complications were hysterectomy, laparotomy, bleeding >1,000 mL, or blood transfusion.

Birch Petersen K et al Fertil Steril. 2016 Jan 18. pii: S0015-0282(15)02310-9. doi: 10.1016/j.fertnstert.2015.12.130. [Epub ahead of print]

Timor-Tritsch & Monteagudo

Cesarean scar pregnancy: a systematic review of treatment studies.

RESULTS : 52 studies included: 4 randomized, controlled trials and 48 case series.

- 15 of 52 analyzed studies scored as high quality.
- Treatment modalities condensed to 14 approaches
- Combining study quality, level of evidence, efficacy, and safety, 5 approaches for treating CSP recommended, depending on availability, severity of patient symptoms, and surgical skills:
  - [1] resection through a transvaginal approach,
  - [2] laparoscopy,
  - [3] UAE in combination with D&C and hysteroscopy,
  - [4] UAE in combination with D&C,
  - [5] hysteroscopy.

Birch Petersen K, et al Fertil Steril. 2016 Jan 18. pii: S0015-0282(15)02310-9. doi: 10.1016/j.fertnstert.2015.12.130. [Epub ahead of print]

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CONCLUSION(S):

- This review recommends treatment options for CSP in clinical practice, based on efficacy and safety.
- The literature supports an interventional rather than medical approach.
- Present recommendations are primarily based on case series.
- Multicenter, well-designed studies are needed to draw definite conclusions on how to treat CSP.

Timor-Tritsch & Monteagudo

CSP: Summary and conclusions

1. The diagnosis of CSP is difficult.
2. CSP is often misdiagnosed as "low intrauterine pregnancy," "cervical pregnancy," or "miscarriage in progress."
3. The best diagnostic tool is high frequency transvaginal ultrasound
4. MRI does NOT add to the Dx.
5. The earlier the diagnosis was established, the better the outcome seemed to be

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6. If possible, sharp curetting should be avoided, it can cause profuse bleeding and, loss of the uterus. If still the choice: have blood and Foley catheter available
7. Systemic MTX as a one shot single agent treatment should be avoided.
   Good adjuvant to other treatments
8. UAE as single agent treatment should be used sparingly or not at all.
   Good adjuvant to other treatments or to save the uterus

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9. Early recognition of CSP and of early PA starts with patient education.

At the time of discharging women from the hospital after a CD, patients should be advised that in a future pregnancy, an early visit (1-2 weeks after a missed period) at the obstetrician for a TVS is of paramount importance.

Recurrent CSP is about 1%!!

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Since Cesarean Scar Pregnancy is one of the precursors of Morbidly Adherent Placentae, the next section is devoted to that subject

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Terms in the literature .....

Placental Attachment Disorders (PAD)

aka: Morbidly Adherent Placenta (MAP)

aka: Abnormal Invasive Placenta (AIP)

aka: Placenta accreta, increta & percreta

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PAD as a Major Health Care Problem

- PAD account for 33-50% of emergency peripartum hysterectomies *
- The consequences are:
  - Cesarean hysterectomy (loss of fertility)
  - Increased rate of blood loss & transfusion
  - Increased rate of ICU admission
  - Injury of adjacent organs

*Habek D, Becarevic R. Fetal Diagn Ther 2007;2:135-7
*Rachman I et al. J Obstet Gynecol2008;2869-72
*GlazeS et al Obstet Gynecol 2008;111:732-8
* Esakoff TF et al Obstet Gynecol 2011;37:324-7

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Risk factors:

- Most common risk factors:
  - Placenta previa
  - Previous cesarean delivery
  - Age
- Others
  - Asherman syndrome
  - Endometrial ablation
  - IVF pregnancy
  - Any intrauterine surgery/manipulation

Timor-Tritsch & Monteagudo

The goal

To review the two major diagnostic modalities: Ultrasound and MRI used at the present time to attempt the most precise prenatal diagnosis

The reason

There were significant changes in the past several years in the evidence for various techniques used to make the diagnosis. Also new clinical and histologic data about PAD

The three clinical forms of PAD

- **In the 1st Δ: Cesarean scar pregnancy**
- **In the 2nd Δ: "Early" placenta accreta**
- **In the 3rd Δ: Placenta accreta, increta, percreta**
- **Each has its own sonographic appearance, clinical signs, natural history and clinical consequence**
- **Each could be considered a different clinical entity, however there is proof that they are expressions of the same histopathologic entity**

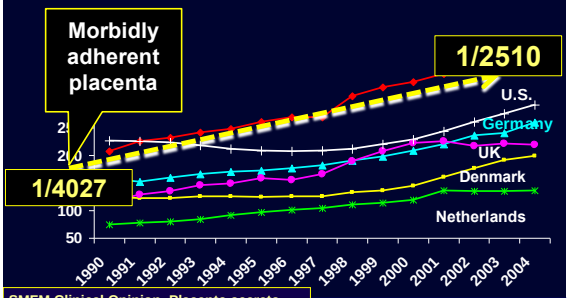
PAD as a Major Health Care Problem

- **PAD account for 33-50% of emergency peripartum hysterectomies ***
- **The consequences are:**
  - **Cesarean hysterctomy (loss of ferility)**
  - **Increased rate of blood loss & transfusion**
  - **Increased rate of ICU admission**
  - **Injury of adjacent organs**

*Habek D, Becarevic R. Fetal Diagn Ther 2007;2:135-7
*Rachman I et al. J Obstet Gynecol2008;2869-72
*GlazeS et al Obstet Gynecol 2008;111:732-8
* Esakoff TF et al Obstet Gynecol 2011;37:324-7

The main & necessary statistics

Cesarean Rates (per 1,000 births), Industrialized Countries,1990-2004



SMFM Clinical Opinion. Placenta accreta. Am J Obstet Gynecol 2010; 203:430–9.

Source: OECD Health Data 2006

Definition, prevalence and relative incidence of MAP

- Accreta (80%) 16
  Superficial myometrial invasion of chorionic villi
- Increta (15%) 3
  De… li
- P…
  Inv… ire
  m… der)

2016 ??

The reported incidence of placenta accreta has increased from approximately *0.8 per 1000* deliveries in the 1980s to *3 per 1000* deliveries in the past decade.

Am J Obstet Gynecol 1977;137: 210

Risk of placenta accreta

	With previa	Without previa
0 prior CS	1-5%	n/a
1 prior CS	11-25%	0.4%
2 prior CS	35-47%	0.6%
3 prior CS	40%	2.4%
4 prior CS	50-67%	n/a

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Theories of pathogenesis.

Previous uterine surgery or uterine interventions: lead to thin or absent decidua basalis and the Nitabuch fibrinoid layer in scarred areas of the lower uterine segment

Clin Perinatol 2008;35:519-29

Timor-Tritsch & Monteagudo

Ultrasound in the Second and Third Trimester

ACOG Committee Opinion. #529, July 2012.

Timor-Tritsch & Monteagudo

Ultrasound signs of MAP

- Four GRAY SCALE markers
  - Clear space
  - Bladder line interruption
  - Lacunae
  - Myometrial thickness
- Two COLOR DOPPLER markers
  - Irregular tortuous vessel crossing the width of placenta
  - Hypervascularity of uterine serosa-bladder wall interface
- COMBINATION of the above

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Gray scale signs

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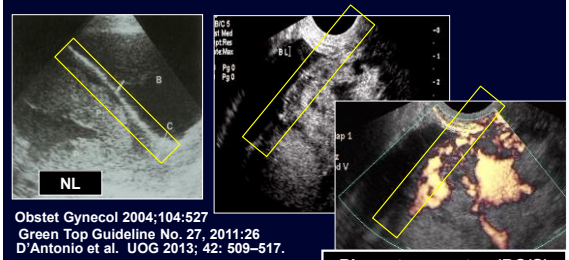
1. Gray scale US: 'clear space'

- In normal placentation: a hypoechogenic space between the placenta & myometrium
- In MAP: Loss of normal hypoechoic zone



Obstet Gynecol 2004;104:527
Green Top Guideline No. 27, 2011:26
D'Antonio et al. UOG 2013; 42: 509–517.

Timor-Tritsch & Monteagudo

Gray scale signs: 'clear space'

Thinning/disruption/disappearance of the hypoechoic interface between the uterus and bladder

Finberg HJ et al JUM 1992;11;333

Timor-Tritsch & Monteagudo

Utility of the 'clear space' in Dx of MAP

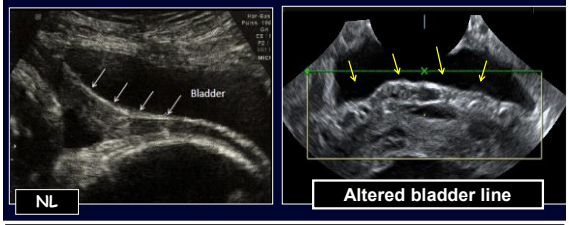
Author	Sensitivity (%)	Specificity (%)	PPV	NPV
Comstock*	73		14	
Wong^	100	35	20	100
Cali~	90	81	57	97
D'Antonio	66.7	95.8		

* Comstock CH, Love JJ, Bronsteen RA, Lee W, Vettraino IM, HuangRR, et al. Sonographic detection of placenta accreta in the 2nd & 3rd trimesters of pregnancy. AJ OG 2004;190:1135
^ Wong HS, Cheung YK, Zucollo J, Tait J, Pringle KC. Evaluation of sonographic diagnostic criteria for placenta accreta. J Clin Ultrasound 2008;36:551–9.
~ Cali G, Giambanco L, Puccio G, Forlani F. Morbidly adherent placenta: evaluation of ultrasound diagnostic criteria and differentiation of placenta accreta from percreta. UOG 2013;41:406–12.
D'Antonio et al. Ultrasound Obstet Gynecol 2013; 42: 509–517.

Timor-Tritsch & Monteagudo

2. Gray scale sign:'Bladder line' interruption

Loss of the normal bladder line



Best seen with 300ml urine/fluid in bladder!!!

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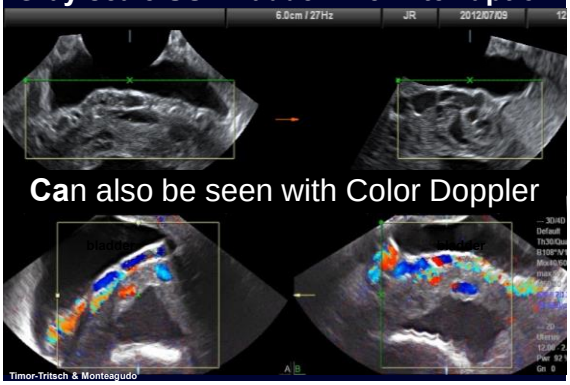
Gray scale US:'Bladder line' interruption



Can also be seen with Color Doppler

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Utility of the 'bladder line' in Dx of MAP

Author	Sensitivity (%)	Specificity (%)	PPV	NPV
Comstock*	20		75	
Wong^	11	100	100	88
Cali~	70	99	96	92
D'Antonio	49.7	99.75		

Probably one of the 3 best US marker of MAP

Comstock CH, Love JJ, Bronsteen RA, Lee W, Vettraino IM, Huang RR, et al. Sonographic detection of placenta accreta in the 2nd & 3rd trimesters of pregnancy. AJ OG 2004;190:1135
Wong HS, Cheung YK, Zucollo J, Tait J, Pringle KC. Evaluation of sonographic diagnostic criteria for placenta accreta. J Clin Ultrasound 2008;36:551–9.
Cali G, Giambanco L, Puccio G, Forlani F. Morbidly adherent placenta: evaluation of ultrasound diagnostic criteria and differentiation of placenta accreta from percreta. UOG 2013;41:406–12.
D'Antonio et al.. Ultrasound Obstet Gynecol 2013; 42: 509–517

Timor-Tritsch & Monteagudo

3. Gray scale sign: 'Lacunae'

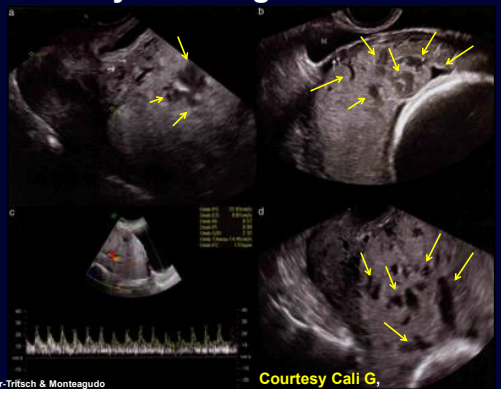
Intraplacental vascular lacunae.

- Grey-scale : Irregular shape not round as placental lakes (Swiss cheese appearance).
- Doppler: Turbulent, pulsatile, low resistance , high velocity jet-like blood flow extending from the placenta into the surrounding uterine or cervical tissues.
- They are located deep in the placenta, (not under the fetal surface of the placenta)

Guy GP, Timor-Tritsch IE et al. AJOG 1990;163:723
Lerner JP, Timor-Tritsch et al UOG 1995;5:198
Finberg HJ et al JUM 1992;11;333
Cali G et al , UOG 2013;41:406–12.

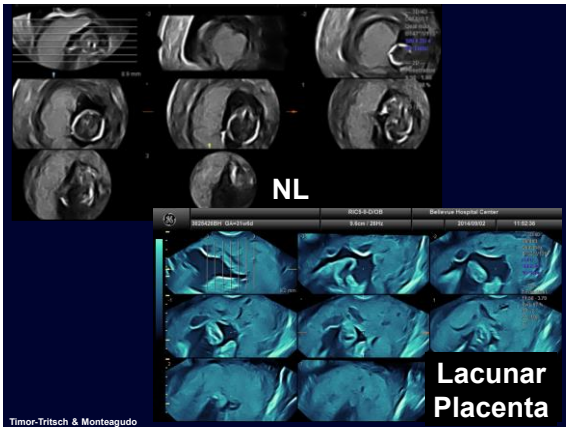
Timor-Tritsch & Monteagudo

3. Gray scale sign: 'Lacunae'



Courtesy Cali G,

Timor-Tritsch & Monteagudo



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Gray scale sign: 'Lacunae'

- The more lacunae the more likely it is placenta percreta.
- Finberg et al (scale 1 to 3);
- Yang et al (grades 0 to 4);
- Cali et al (6 or more = percreta in 100%);

-Finberg HJ, Williams JW. Placenta accreta: prospective US diagnosis in patients with placenta previa and prior cesarean section. J Ultrasound Med 1992;11:333

-Yang JI, Lim YK, Kim HS, Chang KH, Lee JP, Ryu HS. Sonographic findings of placental lacunae and the prediction of adherent placenta in women with placenta previa totalis and prior Cesarean section. UOG 2006;28:178–82

~-Cali G, Giambanco L, Puccio G, Forlani F. Morbidly adherent placenta: evaluation of ultrasound diagnostic criteria and differentiation of placenta accreta from percreta. UOG 2013;41:406–12

- Chen YJ, Wang PH, Liu WM, Lai CR, Shu LP, Hung JH. Placenta accreta diagnosed at 9 weeks' gestation. Ultrasound Obstet Gynecol 2002;19:620–2.

Timor-Tritsch & Monteagudo

Utility of 'lacunae' in Dx of MAP

Author	Sensitivity (%)	Specificity (%)	PPV	NPV
Comstock*	93		93	
Wong^	100	28	21	100
Cali~	73	86	60	90
Yang (Gr ≥1)	87	79	77	88
Yang (Gr ≥2)	100	98	94	100
D'Antonio	77.4	95.1		

Gr 1 = grade 1 (one to three lacunae), Gr. 2 = four to six lacunae

* Comstock CH, Love JJ, Bronsteen RA, Lee W, Vettraino IM, HuangRR, et al. Sonographic detection of placenta accreta in the 2nd & 3rd trimesters of pregnancy. AJ OG 2004;190:1135

^ Wong HS, Cheung YK, Zucollo J, Tait J, Pringle KC. Evaluation of sonographic diagnostic criteria for placenta accreta. J Clin Ultrasound 2008;36:551–9.

~ Cali G, Giambanco L, Puccio G, Forlani F. Morbidly adherent placenta: evaluation of ultrasound diagnostic criteria and differentiation of placenta accreta from percreta. UOG 2013;41:406–12.

D'Antonio et al. Ultrasound Obstet Gynecol 2013; 42: 509–517.

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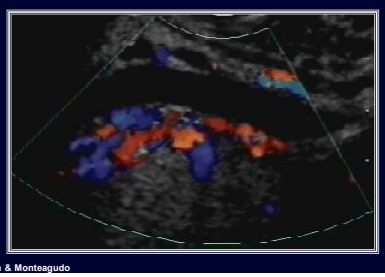
4. Gray scale sign: 'Myometrial thickness' between the placenta and uterine serosa/bladder

- Same value as the 'clear space' represents the same "gray scale" US sign
- The measurement of < 1mm was suggested as indicative of MAP
- Probably the least specific and sensitive sign

Timor-Tritsch & Monteagudo

5. Color/power Doppler signs



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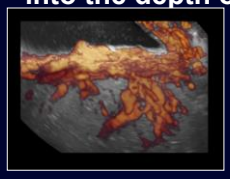
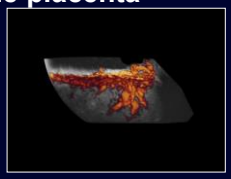
A. Irregular intraplacental tortuous vessels crossing the placental width

Increased vascularity extending from side-to- side, in the width, as well as into the depth of the placenta

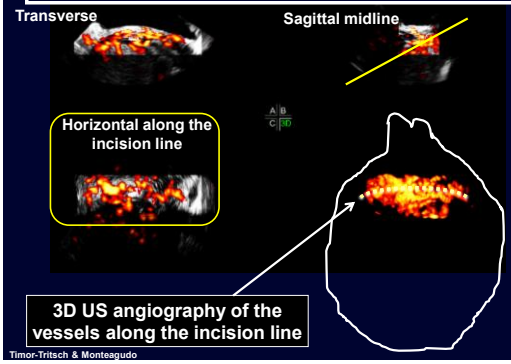




*Cali G, Giambanco L, Puccio G, Forlani F. Morbidly adherent placenta: evaluation of ultrasound diagnostic criteria and differentiation of placenta accreta from percreta. UOG;2013;41:406–12.

Timor-Tritsch & Monteagudo

Demonstration of the vessels along the incision line by using 3D power Doppler display



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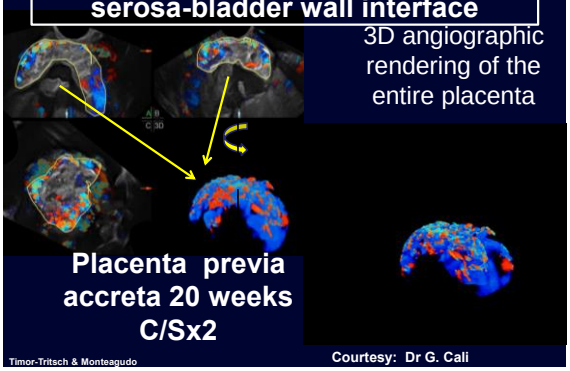
B: Hypervascularity of uterine serosa-bladder wall interface



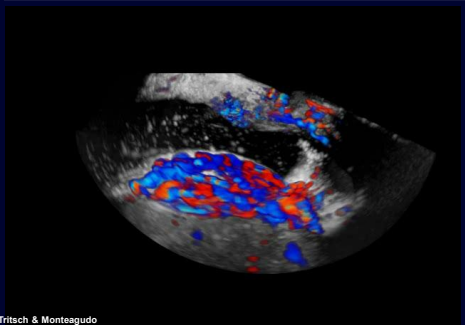
3D angiographic rendering of the entire placenta

Placenta previa accreta 20 weeks C/Sx2

Courtesy: Dr G. Cali

Timor-Tritsch & Monteagudo

B: Hypervascularity of uterine serosa-bladder wall interface



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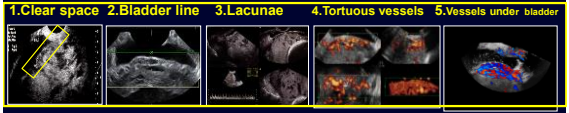
Summary of the sonographic basis diagnosing MAP

Timor-Tritsch & Monteagudo

Number of positive sonographic diagnostic criteria for MAP in 187 patients with placenta previa and history of uterine surgery

Number of criteria	No MAP (n=141)	MAP (n=41)
FIVE	0	8 (all percreta)
FOUR	0	8 ACCR + 8 PERCR
THREE	0	12
TWO	0	5
ONE	49	0
NONE	97	0

1.Clear space 2.Bladder line 3.Lacunae 4.Tortuous vessels 5.Vessels under bladder



G. CALÌ*, L. GIAMBANCO% G. PUCCIOf and F. FORLANI *Ultrasound Obstet Gynecol* 2013; 41: 406-412.

Timor-Tritsch & Monteagudo

Selection of pertinent article regarding sonographic diagnosis of MAP

Timor-Tritsch & Monteagudo

Ultrasound Obstet Gynecol 2016; 47: 290–301
Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.14950

Counseling in fetal medicine: evidence-based answers to clinical questions on morbidly adherent placenta

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- **ABSTRACT**: The goal was to provide up-to-date & evidence-based answers to common clinical questions regarding the diagnosis and management of MAP.
- **US** is the 1ry method for diagnosing MAP with good accuracy.
- **Color Doppler seems to provide the best Dx performance.**
- **MRI** has the same accuracy as US
- **MRI** should be considered when hysterectomy, is planned as it can provide detailed information about the topography of placental invasion and predict difficulties at surgery.

Timor-Tritsch & Monteagudo

Ultrasound Obstet Gynecol 2013; **42**: 509–517
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Prenatal identification of invasive placentation using ultrasound: systematic review and meta-analysis

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- Two authors independently abstracted data from 23 studies of 3707 pregnancies at risk for MAP
- Sensitivity, specificity, positive and negative likelihood ratios (LR+ and LR–), the diagnostic odds ratio(DOR) and their 95% CIs for each study were calculated.

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- **Overall performance of US** for the antenatal detection of invasive placentation was:
  - sensitivity, 90.7% (95% CI, 87.2–93.6);
  - specificity, 96.9% (95% CI, 96.3–97.5);
  - LR+, 11.01 (95% CI, 6.1–20.0);
  - LR–, 0.16 (95% CI, 0.11–0.23); and
  - DOR, 98.5 (95% CI, 48.8–199.0).
- Among the different US signs, **color Doppler had the best predictive accuracy**
  - sensitivity, 90.7% (95% CI, 85.2–94.7);
  - specificity, 87.6% (95% CI, 84.6–90.4);
  - LR+, 7.7 (95% CI, 3.3–18.4);
  - LR–, 0.17 (95% CI, 0.10–0.29); and
  - DOR, 69.0 (95% CI, 22.8–208.9)).

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Pooled values for US overall and the different US signs in the identification of invasive placentation

Dx Method	Studies	Pts	SENS	SPEC	LR+	LR-	DOR
US overall	23	3707	90.7	96.9	11.0	0.16	96.6
Lacunae	13	2775	77.4	95.1	4.5	0.29	24.4
Loss clear space	10	2633	66.7	95.8	5.6	0.38	25.0
Abnormal Bladder Line	9	2579	49.7	99.75	30.6	0.5	93.7
Abnormal Color Doppler	12	714	96.7	87.7	7.77	0.17	69.1

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NIH publication 2014

The NIH consensus panel issued the following statistics for the US Dx of MAP

- Sensitivity 77% (95% CI 60-80%)
- Specificiy 96% (95% CI 93-97%)
- PPV 65% (95% CI 60-80%)
- NPV 98% (95% CI 95-98%)

"US should be the primary tool for the Dx. and can be the only modality in the majority of cases The sensitivity and specificity of MRI is comparable to US

- **MY COMMENT: US markers did not include evaluation of the "bladder line" and " 3D US"**
- **If included, it would have resulted in better metrics**
- **Reason for excluding 3D Doppler was: it is not universally used and its use can not be mandated**

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–Reddy UM, Abuhamad AZ, Levine D, Saade GR Executive Summary of a NICH&HD SMFM, AIUM, ACOG, ACR, SPR, SRU FETAL IMAGING WORKSHOP AJOG 2014

Accuracy of ultrasound for the prediction of placenta accreta

- Objective: To test if previously reported US sensitivity of >90% for Dx of PA is valid
  - - 6 observers blinded to clinical status
  - Design: 1 center, retro study. PA matched c. controls (pts c. previa)
- Results: 229 USs (55 with PA & 56 with previa) 1374 observations
  - 30.8% true positives,
  - 6.7% false positives,
  - 44.2% true negatives,
  - 18.3% false negatives,
  - 12.0% = "unable to be determined,"

Bowman Z et al. Accuracy of predicting placenta accreta AJOG August 2014

Accuracy of ultrasound for the prediction of placenta accreta

Sens: 53.5%,
Spec: 88.1%,
+Pred Val: 82.1%,
- Pred Val: 64.8%,
- Accuracy:65.8%

PA was found to be associated with placental lacunae, loss of retro-placental clear space, irregular bladder wall & abnormalities of color Doppler.

Conclusion: US may not be as sensitive as previously described to predict PA.

Bowman Z et al. Accuracy of predicting placenta accreta AJOG August 2014

Ultrasound predictors of placental invasion: the Placenta Accreta Index

Martha W. F. Rac, MD; Jodi S. Dashe, MD; C. Edward Wells, MD; Elysia Moschos, MD; Donald D. McIntire, PhD; Diane M. Twickler, MD

Am J Obstet Gynecol 2015;212:343.e1-7.

TABLE 3
OR estimates and CIs of each parameter used in Placenta Accreta Index

Parameter	OR	95% CI
Grade-3 lacunae	10.8	1.4–83
No. of cesarean deliveries	9.6	2.5–37.1
Placental location	3.9	1.1–14.1
Grade-2 lacunae	2.9	0.6–12.7
Bridging vessels	2.3	0.6–8.7
Sagittal smallest myometrial thickness	1.0	0.8–1.2

CI, confidence interval; *OR*, odds ratio.

Rac. Placenta Accreta Index. Am J Obstet Gynecol 2015.

For best diagnostic results of MAP

- 1. First evaluate patient risk
- 2. Optimize imaging by using transvaginal US with "comfortably full" bladder (≈ 300cc)
- 3. Use Color Doppler with low pulse repetition frequencies (≈0.9kHz)
- 4. Report findings as: high risk, low risk or intermediate risk for bleeding
  - –If unsure, be conservative: false positive results are acceptable

Modified after A. Abuhamad

Does M R I help?

Three questions

- There are three areas to be addressed when assessing MRI to rule in or out MAP:
  - which is/are the best MRI sign/s,
  - are the sensitivity & specificity of MRI & US comparable, since US is done first (bias??)
  - at what GA can MRI (a more expensive test) contribute additional information.

The best MRI signs MAP

- Dark intra-placental bands* on T2 are most predictive (equivalent to lacunae by US)
- Vessels of 6 mm or greater (presumably correspond to large vessels) .
- Focally interrupted myometrial border.
- Infiltration of pelvic organs.
- Tenting of the bladder
- Placental protrusion into the internal os

* Lax A et al, The value of specific MRI features in the evaluation of suspected placental invasion. Magn Reson Imaging 2007;25:87–93.

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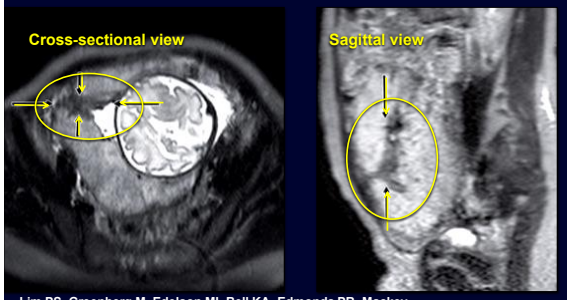
MRI: intraplacntal 'dark bands'



Lim PS, Greenberg M, Edelson MI, Bell KA, Edmonds PR, Mackey AM. Utility of ultrasound and MRI in prenatal diagnosis of placenta accreta: a pilot study. AJR Am J Roentgenol 2011;197: 1506–13.

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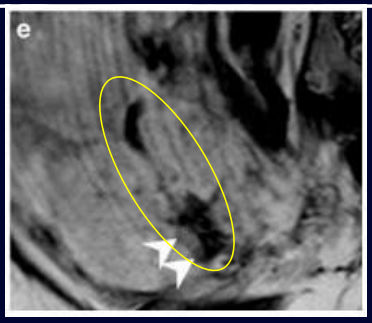
MRI: 'dark bands'



Ueno Y et al. Eur Radiol. 2013 Nov 22. [Epub ahead of print]

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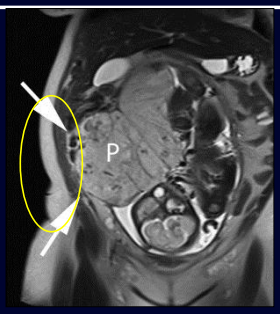
Focally interrupted myometrial border



Allen BC Rads Clin North Am 2013

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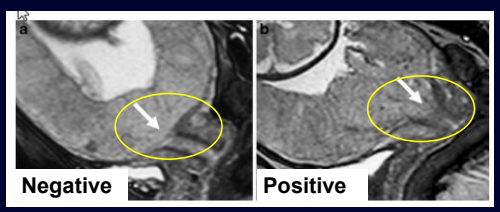
Novel MRI sign: 'placental protrusion sign'

65 patients : MRI (1.5-T unit) coronal & sagittal T2-weighted half-Fourier single-shot turbo spin echo imaging. In 15 pts the Dx was invasive placenta praevia.



Ueno Y et al. Novel MRI finding for diagnosis of invasive placenta praevia: evaluation of findings for 65 patients using clinical and histopathological correlations. Eur Radiol. 2013 Nov 22. [Epub ahead of print]

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The MRI features of placental adhesion disorder and their diagnostic significance: systematic review

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AIM: To identify the most frequently used MRI features in the diagnosis of placenta adhesion disorder (PAD) in the antenatal period and their significance.

Rahaim NS, Whitby EH. The MRI features of placental adhesion disorder and their diagnostic significance: systematic review.Clin Radiol. 2015

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- **RESULTS**: 614 relevant articles identified . Only 11 met the inclusion criteria.
- The commonest MRI criteria used were
  - T2 dark intraplacental bands,
  - heterogeneity of placenta,
  - abnormal uterine bulging, and
  - disruption of the utero-placental zone.
- A newly described criterion is disorganised vasculature of placenta.
- **MRI sensitivity and specificity varied between 75-100% and 65-100% respectively**.

Rahaim NS, Whitby EH. The MRI features of placental adhesion disorder and their diagnostic significance: systematic review.Clin Radiol. 2015

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- **CONCLUSION**: MRI diagnosis of PAD relies on **unstandardised criteria** of diagnosis
- However, it is still **has a high diagnostic accuracy** and frequently aids in surgical planning, supporting US
- Most studies are of a **small sample size.**
- **Additional multicentre studies are recommended** to enhance the generalisability of the findings and asses the value of the newly described criteria

Rahaim NS, Whitby EH. The MRI features of placental adhesion disorder and their diagnostic significance: systematic review.Clin Radiol. 2015

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Why is it hard to evaluate MRI articles?

- Study designs are different with mostly multiple different interpreters
- The low number of women in studies (power)
- A variation of US criteria used for comparison

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Underpowered MRI studies

All studies of comparing MRI vs US are underpowered.

Dwyer et al. calculate that 194 women would need to have both US and MRI in a paired study design to have an 80% power to detect a difference at the P = 0.05 level, and even more women would be needed in an unpaired study design.

--Dwyer BK et al. Prenatal diagnosis of placenta accreta: sonography or magnetic resonance imaging? J U M 2008;27:1275–81.

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The use of MRI in the diagnosis of MAP Conclusions

- MRI is a reasonable diagnostic imaging modality. It is more costly (≈x4) than US
- It requires dedicated expertise
- It is not a primary imaging test
- Its real effectiveness is hard to evaluate, however it is close to that of US
- It should be used if US is inconclusive
- <u>Disadvantage: no blood vessel info!</u>

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Answers to the 3 MRI questions

Q: Which is/are the best MRI sign/s?

A: Probably the dark bands (lacunae on US)

Q: Are the sensitivity & specificity of MRI & US comparable?

A: Yes they are, if US is done first

Q: At what GA can MRI contribute additional information?

A: Inconclusive before 24 wks. The later, the higher the accuracy (still no vessel info)

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Final Conclusions: CSP

- The diagnosis of CSP is difficult.
- CSP is often misdiagnosed as “low intrauterine pregnancy,” “cervical pregnancy,” or “miscarriage in progress.”
- The best diagnostic tool is high frequency transvaginal ultrasound
- MRI does NOT add to the Dx.
- There is no concensus on its management
- If TOP is the choice, procede ASAP
- CSP and MAP share a common histology
- CSP is a precursor of MAP

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Final Conclusions: MAP

- Due to the increase of CDs MAP became almost a daily diagnostic problem of the Ob/Gyn and the imaging laboratories
- Prenatal diagnosis became more reliable due the experience & knowledge gained
- Gray scale, but mostly color Doppler US are the primary, dependable imaging modalities
- If US is inconclusive, MRI helps
- Continuing a CSP can result in a live neonate with risk of a cesarean hysterectomy
- Multidisciplinary treatment approach is imperative!

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