GGG

Narbenschwangerschaft

Ein zunehmendes Problem im klinischen Alltag

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Definition

Implantation of the gestational sac **into** a uterine scar (e.g. from hysterotomy)[1]

Location (mostly) in the lower uterine segment – resulting from cesarean delivery

Different terms in literature[1]:

- *"cesarean scar pregancy – CSP"*
- *"cesarean ectopic pregancy"*
- *"cesarean scar ectopic"*

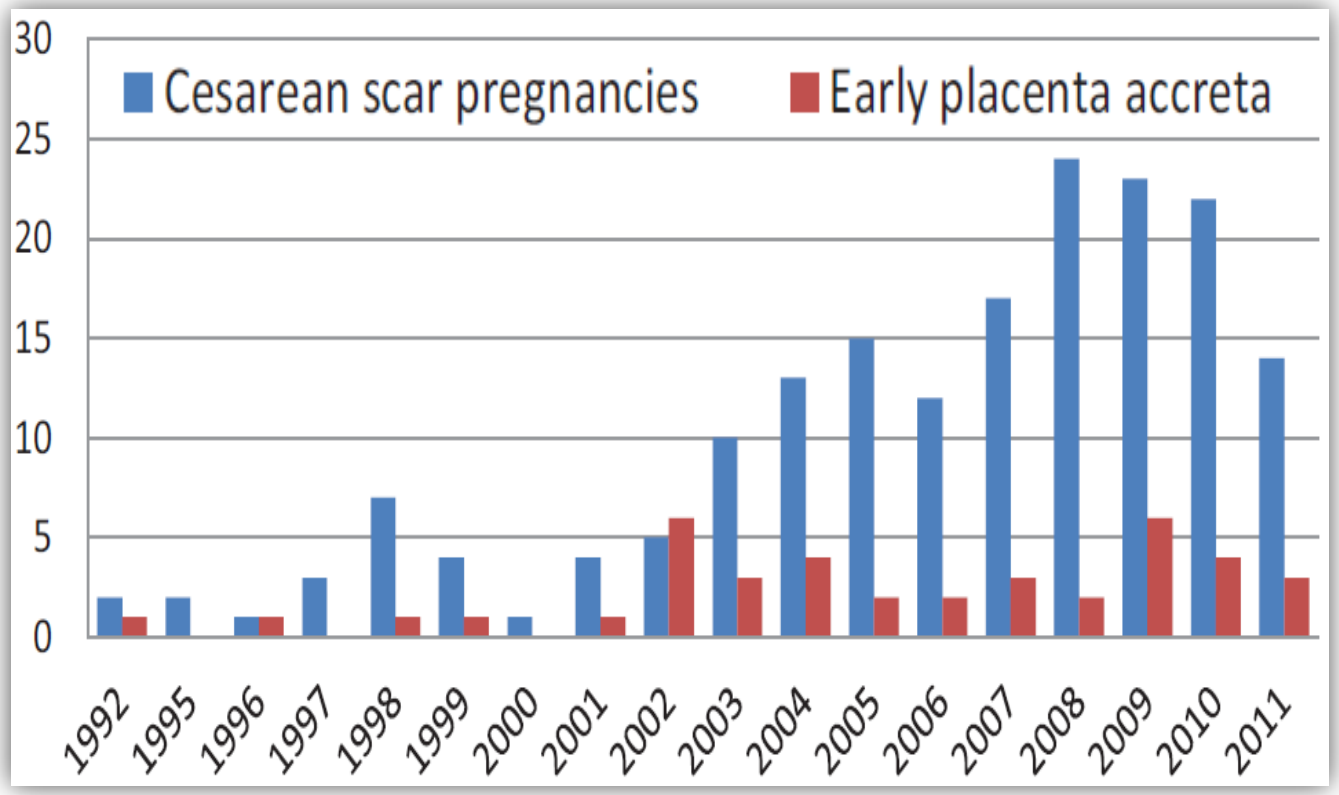
Few data in literature; no RCTs available

[1]Timor-Tritsch IE et al. AJOG (2012)

Definition

First report in 1978 by **Larsen & Solomon**[1]

- 112 cases up to 2002[2]
- 751 cases up to 2012[3]



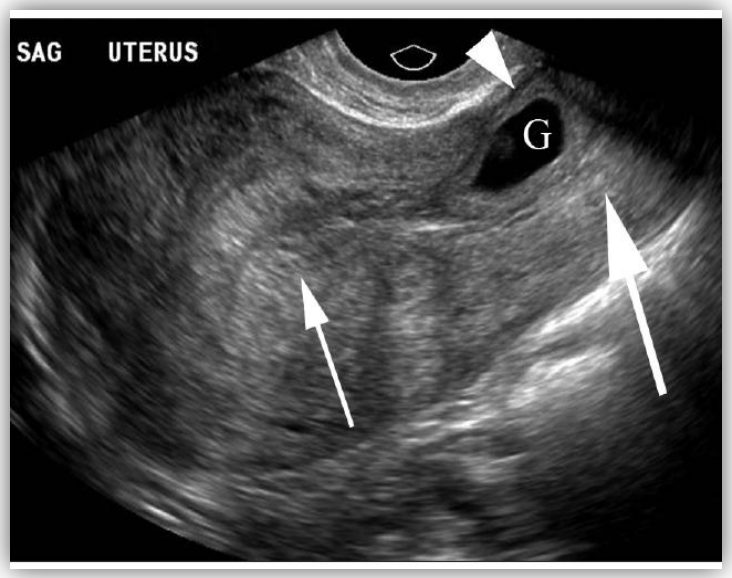
[1]Larsen JV & Solomon MH S Afr Med J (1978),[2]Rotas MA et al. Obstet Gynecol (2006),
[3]Timor-Tritsch IE et al. AJOG (2012)

Is CSP real ectopic?

Since no official definition aggreement …

YES Implantation within fibrous tissue surrounding cesarean scar

NO Implantation within the niche of the cesarean scar, facing uterine cavity



Timor-Tritsch IE, AJOG (2012)

Two Types of CSP

TYPE-1: Implantation on top of the scar, progression towards uterine cavity
(viability achievable, **high risk of bleeding**)

TYPE-2: deep implantation within fibrous tissue of the scar
(**progression towards uterine rupture**)

Vial Y et al. Ultrasound Obstet Gynecol (2000)

Incidence

Incidence ranging from **1:1,800 – 1:2,216**[1]
~ 6.1% of ectopic pregancies (with history of CD)[1]

cervical pregancy incidence 1:2,000 – 1:18,000[2]

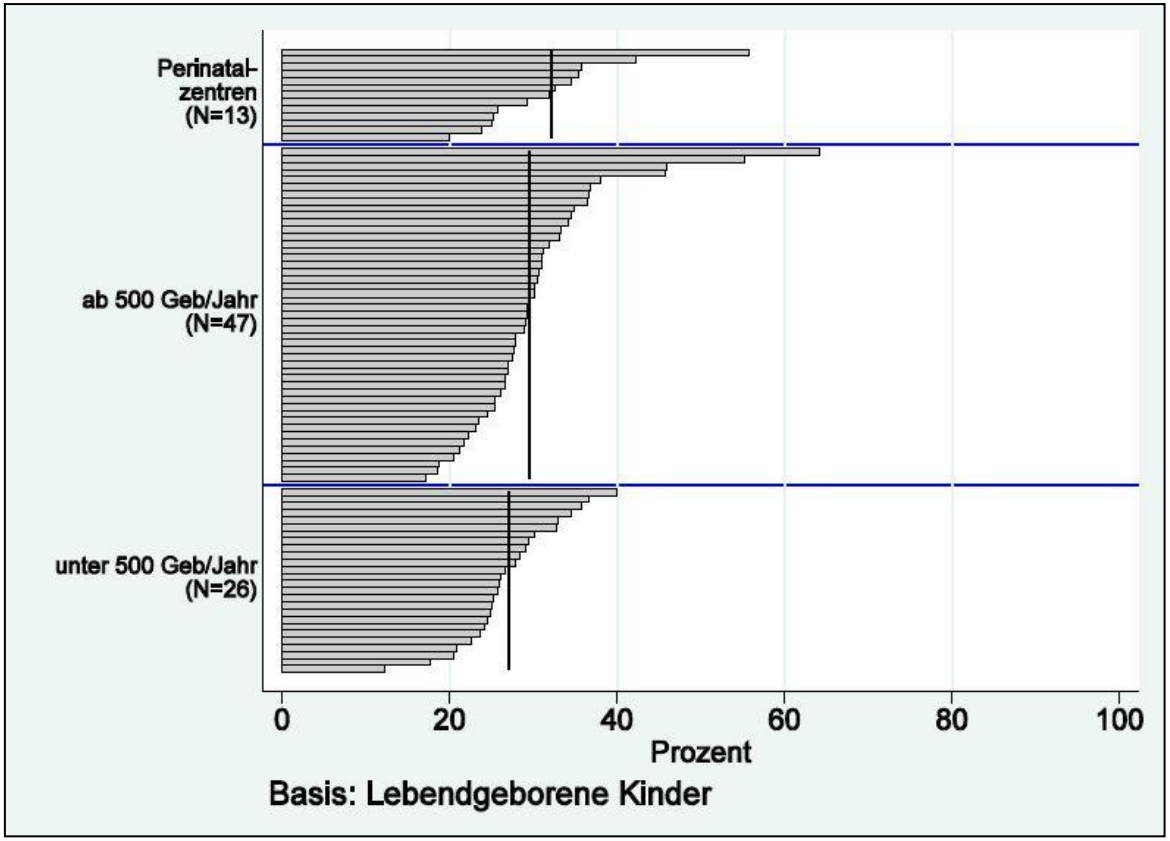
Correlation to rising incidence of CD over the last decade?

Since 1996 increase of CD approximately 40% in US; 2007 **31.8%**[3]

- Increase of primary CD (12.6% > 20.6%)
- Decrease of vaginal delivery after primary CD (28% > 9.2%)

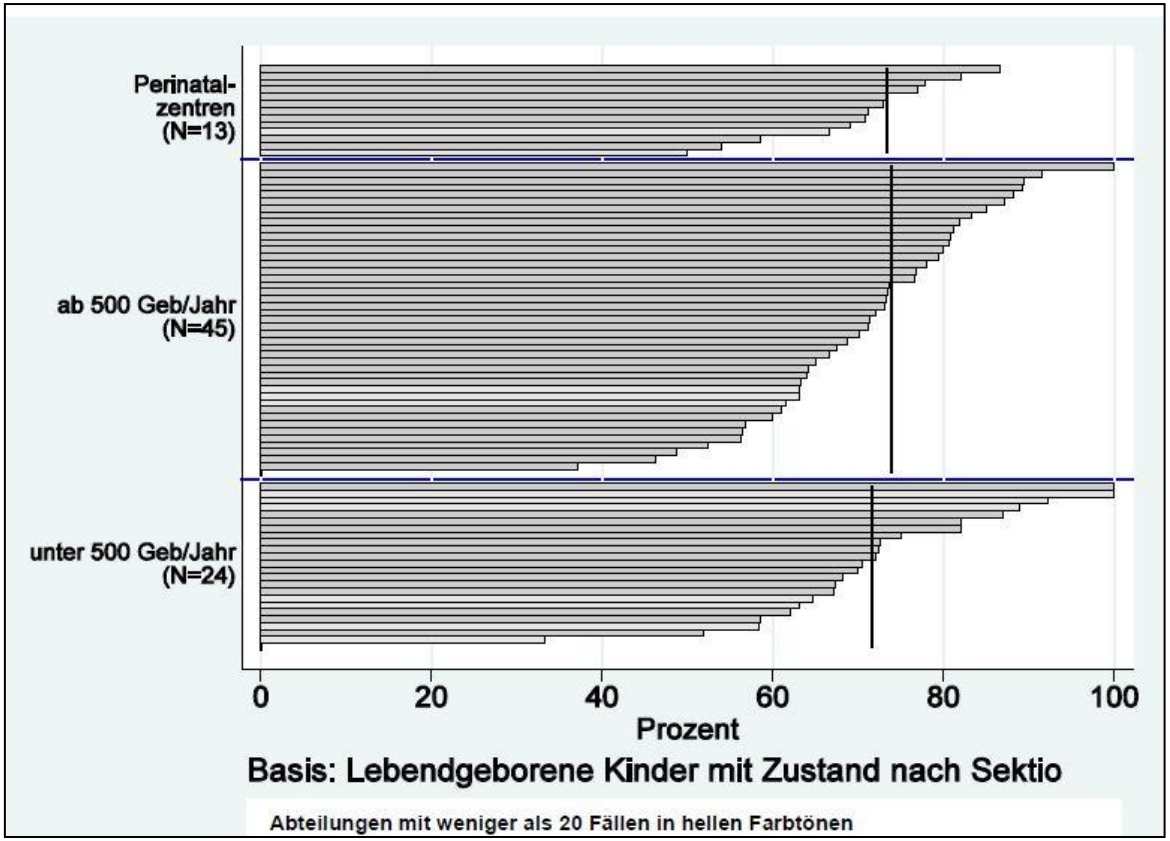
[1]Jurkovic D et al. Ultrasound Obstet Gynecol (2003), [2]Yankowitz J et al. Obstet Gynecol Surv (1990),
[3]Hamilton BE Natl Vital Stat Rep (2007)

One out of three deliveries by Caesarean



23,675 CD in 2012 in AUT
(30% of all deliveries)

73% of deliveries by Caesarean (status post CD)

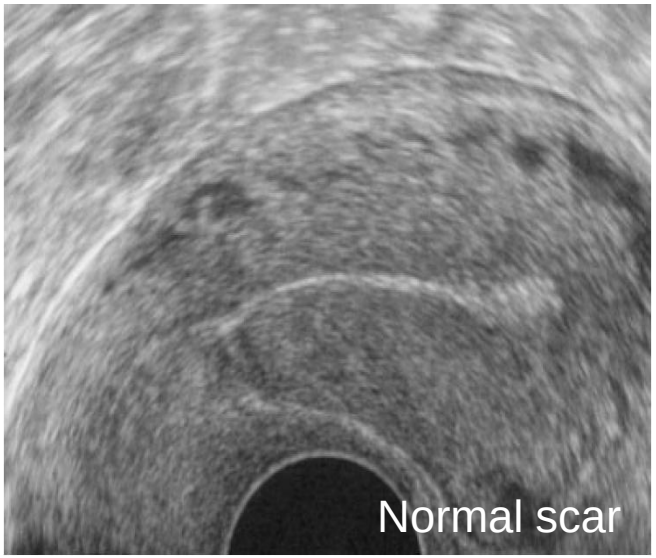


Pathogenesis of „real“ ectopic CSP (Type-2)

Invasion of conceptus may occur through a microscopic dehiscence or defect in the scar

- **poor vascularization**
- **fibrosis, incomplete healing**

Generally accepted pathophysiologic approach for all intramural pregancies
(curetage, myomectomy, endometriosis interna, manual removal of placenta)



Chen HY Ultrasound Med Biol (1990) – N=47 (3mos after CS)
50% normal pattern; 50% showed thinned low uterine segment (< 3.5mm) & defects

Jurkovic D et al. Ultrasound Obstet Gynecol (2003)

Etiology & Risk factors (I)

Increased risk by multiple cesarean sections?

Rationale: Increment of scar surface; impaired wound healing (minor vascularization, fibrosis)

Osser OV et al. UOG (2009) – N=287
(TVS 6-9 mos after delivery)

Finding	*Vaginal delivery (n = 125)*	*One CS (n = 108)*	*Two CS (n = 43)*	*Three or more CS (n = 11)*	P
Uterus in anteflexion	104 (83)	86 (80)	33 (77)	10 (91)	—
One visible scar	0 (0)	108 (100)	16 (37)	2 (18)	—
Two visible scars	0 (0)	0 (0)	27 (63)	9 (82)	—
At least one scar with a defect	0 (0)	66 (61)	35 (81)	11 (100)	0.002*
At least one scar with a large defect (subjective evaluation)	0 (0)	15 (14)	10 (23)	5 (45)	0.027*
At least one scar with a total defect (subjective evaluation)	0 (0)	7 (6)	3 (7)	2 (18)	0.336*
Myometrial thickness in the isthmus uteri (mm)					
Median (range)	11.6 (7.9–17.3)	8.3 (3.8–15.0)	6.7 (3.6–10.7)	4.7 (2.4–8.0)	< 0.001†
25th, 75th percentiles	10.1, 12.9	7.1, 9.5	5.3, 7.8	3.0, 6.0	
Myometrial thickness in the isthmus uteri ≤ 5mm	0 (0)	2 (2)	8 (19)	6 (55)	< 0.001†

Etiology & Risk factors (II)

Increased risk by multiple cesarean sections?

- **Scars with defects located lower in the uterus**

  Median distance intact scar – internal cervical os: 4.6 mm (0-19)
  Median distance defect scar – internal cervical os: 1.0 mm (0-26)

- **Higher risk after secondary cesarean**

  Dilatation of lower uterine segment?

Indication	n	%
Breech presentation	11	31.4
Fetal distress	8	22.9
Arrest of labor	7	20
Preeclampsia	4	11.4
Placenta previa	3	8.6
Twin gestation	2	5.7

Rotas MA et al. ACOG (2006)

Maymon R et al. Hum Reprod Update (2004)

Undeveloped lower uterine segment in case of Breech presentation?

Osser OV et al. UOG (2009)

Etiology & Risk factors (III)

Relevance of Surgical Technique?

Single layer vs. double layer / locked vs. unlocked

Growing body of evidence that surgical technique influences short-term and long-term outcome.

Roberge S et al. IJGO (2011) – Meta-Analysis (160 cases of uterine rupture; retrosp.)

- Single-layer (locked) increased risk of uterine rupture (OR 4.96; p<.001)
- Single-layer (unlocked) no increased risk (OR 0.49; p<.10)

Impact of single- vs double-layer closure on adverse outcomes and uterine scar defect: a systematic review and metaanalysis AJOG (2014)

Stéphanie Roberge, MSc; Suzanne Demers, MD; Vincenzo Berghella, MD; Nils Chaillet, PhD; Lynne Moore, PhD; Emmanuel Bujold, MD, MSc

Systematic Rev. + Meta-Analysis (N=20 (6 of them randomized trials)

Single-layer vs. Double-layer

Impact of single- vs double-layer closure on adverse outcomes and uterine scar defect: a systematic review and metaanalysis AJOG (2014)

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TABLE 2
Impact of single- vs double-layer closure on risk of maternal outcome

Outcome	No. of trials	No. of participants	Prevalence: Single layer (%)	Prevalence: Double layer (%)	RR (95% CI)	*P* value	I^2
Maternal infectious morbidity	10	5868	416/2937 (14.2)	425/2931 (14.5)	0.92 (0.74–1.15)	.48	37%
Endometritis	8	13,815	196/6907 (2.8)	183/6908 (2.6)	1.04 (0.81–1.34)	.76	26%
Wound infection	8	13,730	566/6856 (8.3)	612/6874 (8.9)	0.93 (0.83–1.04)	.18	15%
Blood transfusion	7	14,313	141/7149 (2.0)	164/7164 (2.3)	0.86 (0.69–1.08)	.19	23%
			Means		Mean difference (95% CI)		
Mean blood loss, mL	6	1025	473	513	−40 (−110 to 29)	.26	95%
Duration of cesarean, min	9	4722	33.5	39.7	−6.1 (−8.7 to −3.4)	< .0001	94%
Hospital stay, d	5	4063	4.2	4.6	−0.3 (−0.7 to 0.0)	.05	85%

CI, confidence interval; *RR*, risk ratio.

Roberge. Uterine closure and adverse maternal outcomes. Am J Obstet Gynecol 2014.

Single-layer vs. Double-layer

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TABLE 3
Single- vs double-layer closure on risk of scar defect and lower uterine segment thickness

Outcome	No. of trials	No. of participants	Prevalence		RR (95% CI)	*P* value	I^2
			Single layer (%)	Double layer (%)			
Scar defect evaluated by US	3	193	25/100 (25.0)	57/93 (61.3)	0.53 (0.24–1.17)	.12	67%
Uterine rupture or dehiscence	2	187	4/83 (4.8)	3/104 (2.9)	2.38 (0.63–8.96)	.20	0%
			Means		Mean difference (95% CI)		
LUS thickness, mm	2	240	15.0	17.6	−2.6 mm (−3.1 to −2.2)	< .0001	0%

CI, confidence interval; *LUS*, low uterine segment; *RR*, risk ratio; *US*, ultrasound.

Roberge. Uterine closure and adverse maternal outcomes. Am J Obstet Gynecol 2014.

Double-layer = myo thickness increase

Locked vs. Unlocked

- No difference in risk of uterine scar defect (RR 2.14; p=.51)
  double-layer 1st locked vs. 1st unlocked

- Decreased myometrium layer (-2.5 mm; p<.01); increased blood loss (+45.0ml; p<.001)
  double-layer (1st locked)

Yasmin S et al. JCPSP (2011)

- No difference in proportion of scar defects (US 6-12 mos post CD) (RR 1.16; p=.11)
  single-layer locked vs. unlocked

- Larger scar defect in **single-layer locked** (p<.001)

Ceci O et al. J Obstet Gyn Res (2012)

"… Final recommendation due to lack of data (RCT, larger collectives) not possible …" Bij de Vaate AJM et al. UOG (2014)

Diagnosis of uterine scar defects (I)

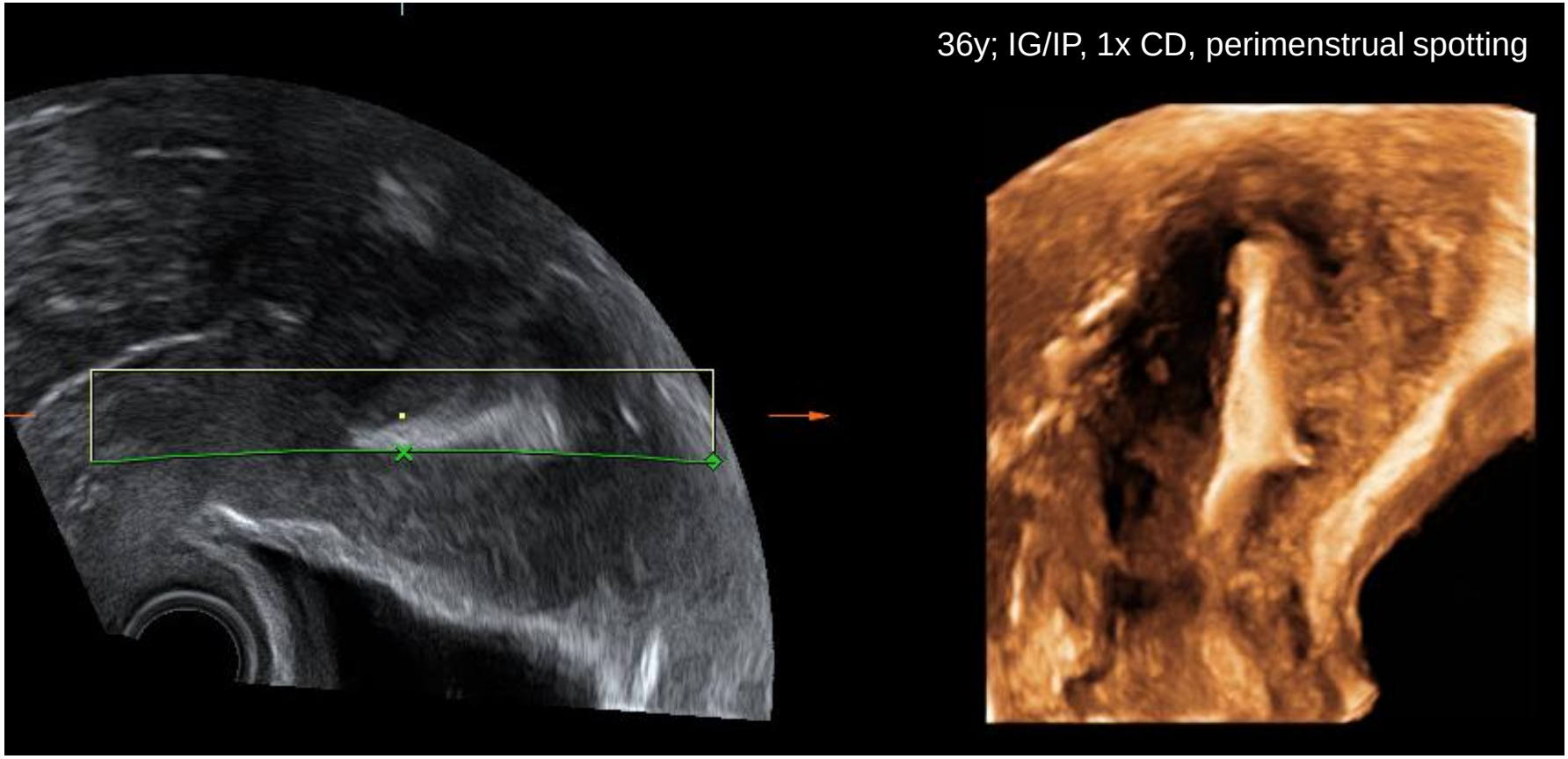
clinical sign – **bleeding irregularities**[1]

N = 71 (at least on CD in anamesis) - 29 (40%) showing “scar defects”

- All women reported *prolonged periods or post-menstrual spotting.*
- Clinic was correlating with wide of scar defect
- Hypothesis: Minor contractility around scar > retention of blood[2]

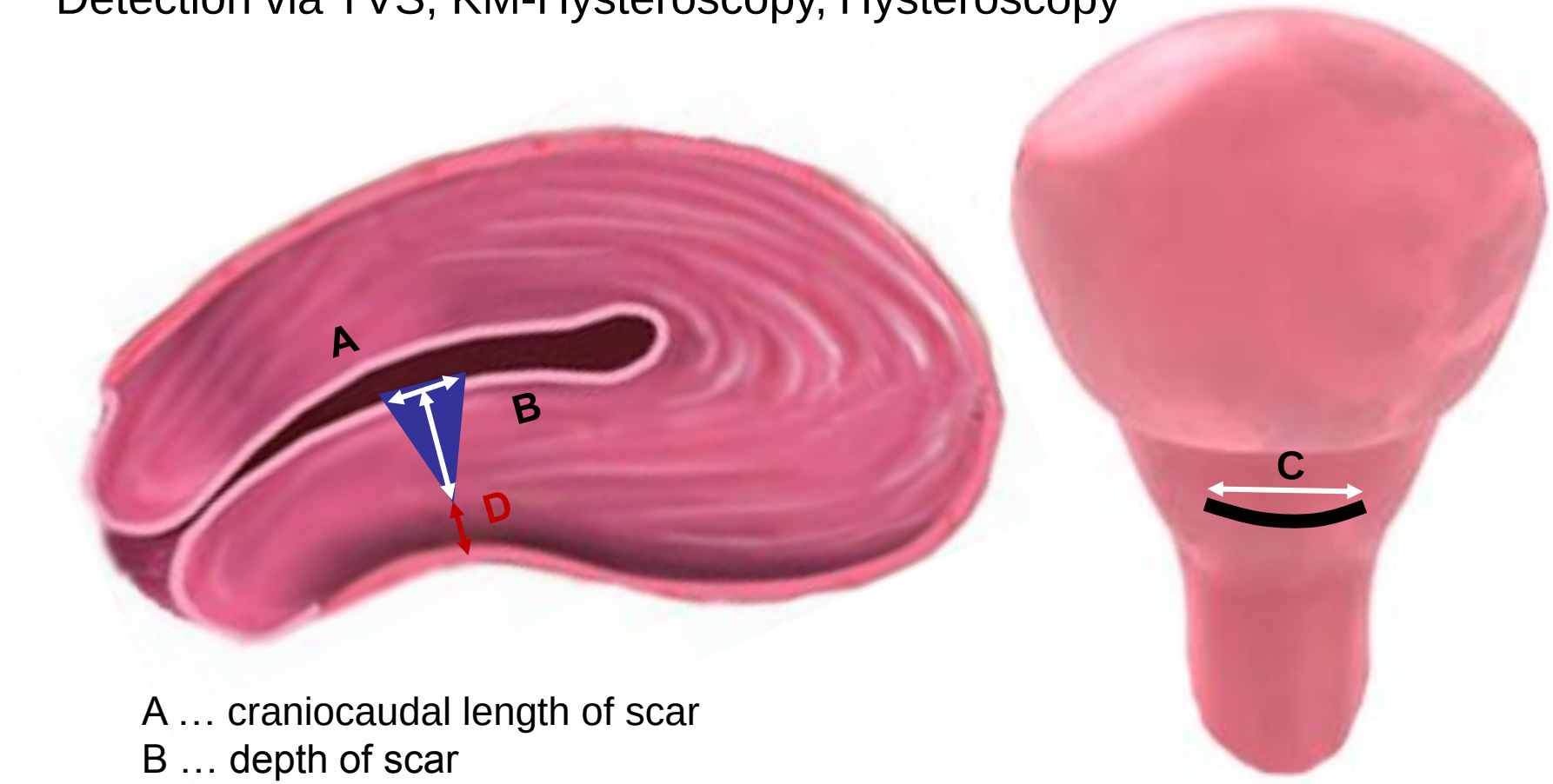
[1]Uppal D et al. J Obstet Gynecol (2011), [2]Thurmond AS J Ultrasound Med (1999)

Diagnosis of uterine scar defects (I)



Diagnosis of uterine scar defects (II)

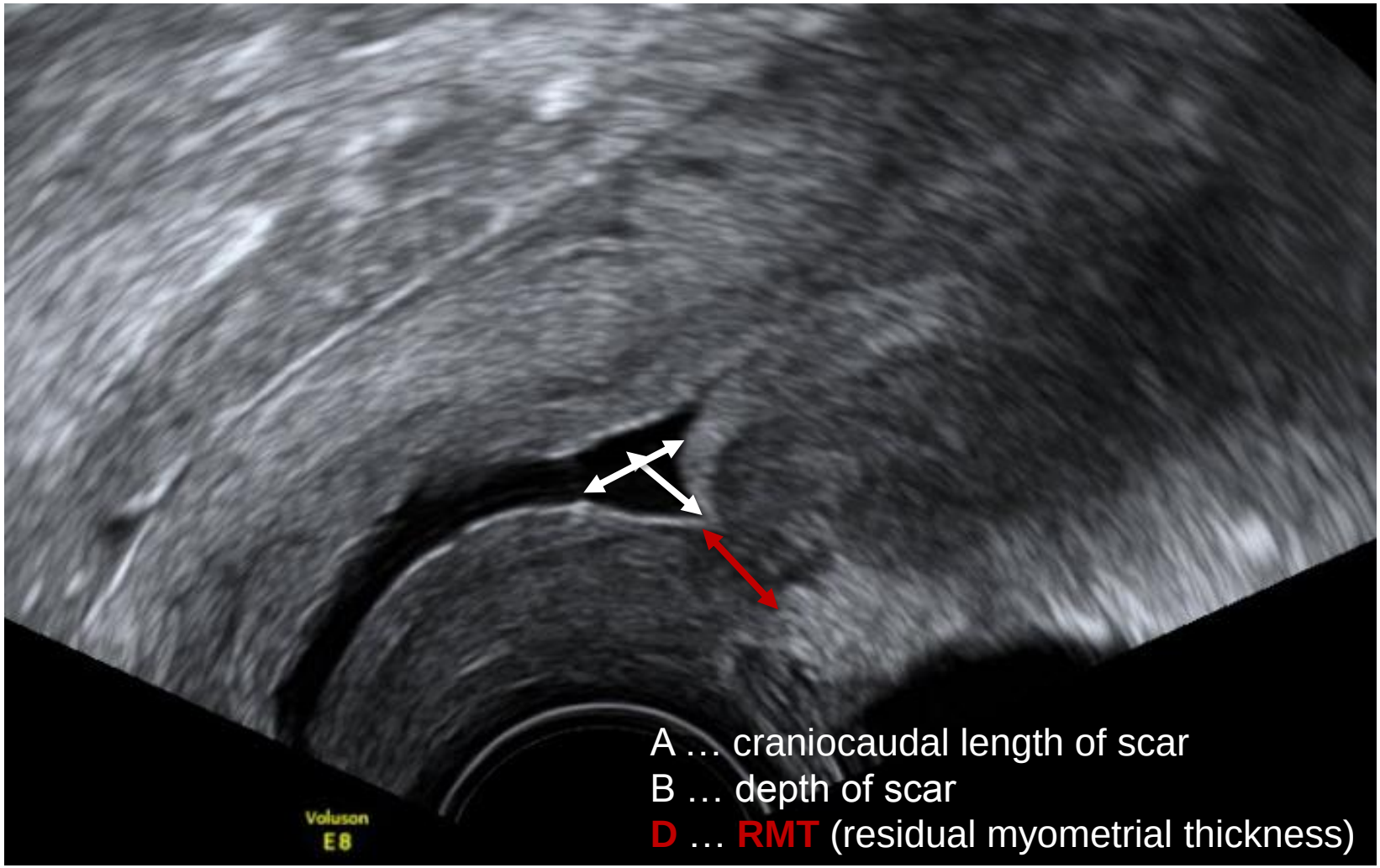
Detection via TVS, KM-Hysteroscopy, Hysteroscopy



A … craniocaudal length of scar
B … depth of scar
C … wide of scar (vertical)
D … **RMT** (residual myometrial thickness)

Naji O Hum Reprod (2012)

Diagnosis of uterine scar defects (III)



Diagnosis of Cesarean Scar Pregenancy

Presenting Symptom	n	%
Asymptomatic	21	36.8
Painless vaginal bleeding	22	38.6
Abdominal pain and bleeding	9	15.8
Abdominal pain	5	8.8

Rotas MA et al. Obstet Gynecol (2006) – N=57

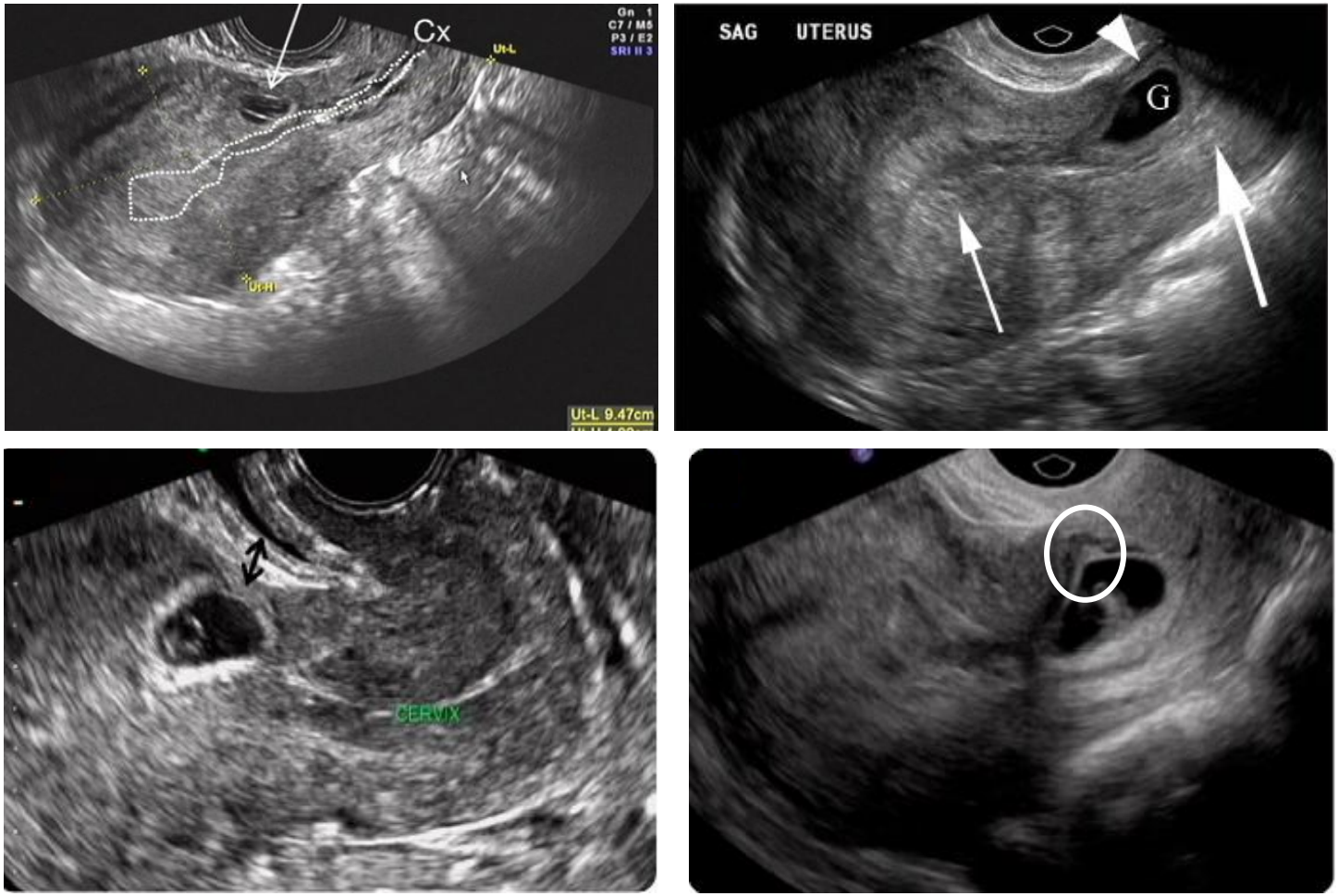
TVS first choice tool!

1. Empty uterine cavity and empty endocervical canal / closed cervical canal
2. Detection of GS and/or placenta embedded **in** hysterotomy scar – TYPE 1
3. Triangular GS fills the niche of scar (only before 8 week pm) – TYPE 2
4. Thin (1-3 mm) or absent myometrial layer towards bladder
5. Presence of prominent vascular pattern at or in CD scar area (+ HCG positive)

   (low impedance (pulsatility <1), high-velocity flow (> 20cm/s))

Osborn DA et al. J Ultrasound Med (2012), Timor-Tritsch IE et al. AJOG (2012)

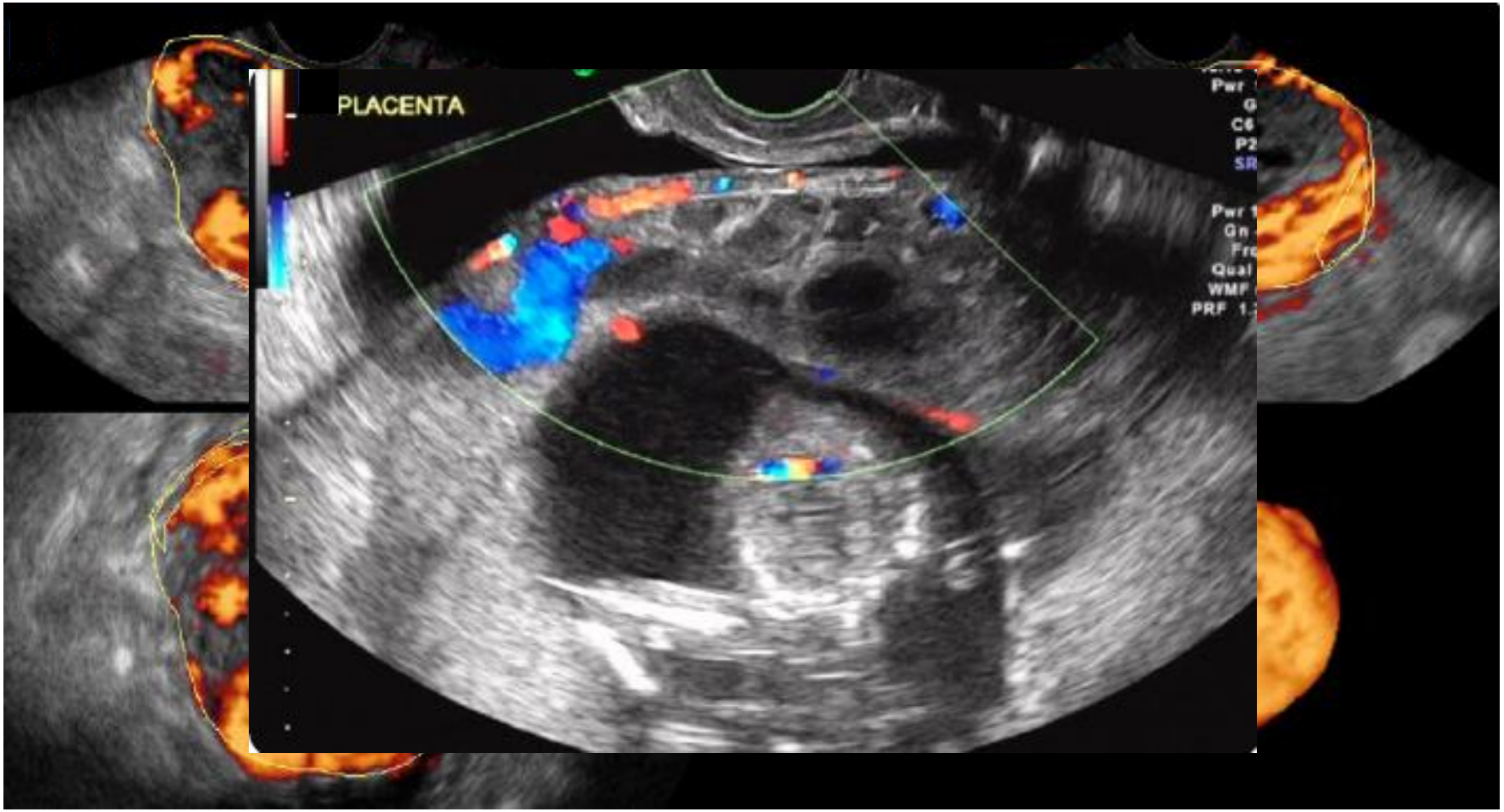
Diagnosis of Cesarean Scar Pregenancy



Sensitivity (first trimester) – 86.4%[1]

Osborn DA et al. J Ultrasound Med (2012), Timor-Tritsch IE et al. AJOG (2012);
[1]Ash A et al. BJOG (2007)

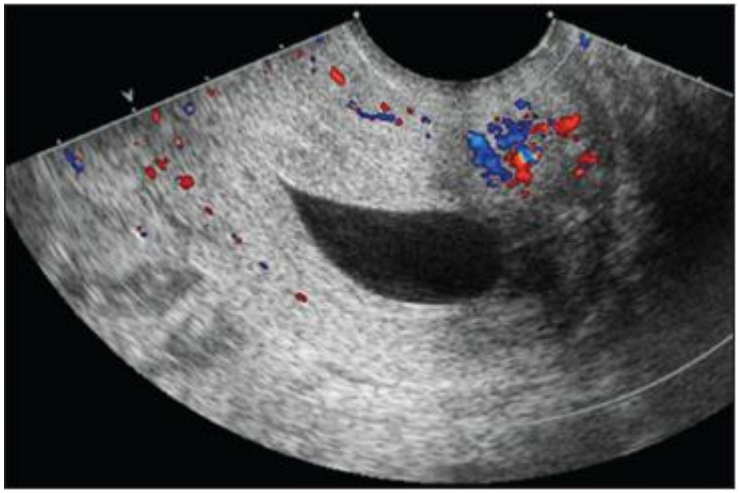
Diagnosis of Cesarean Scar Pregenancy



Timor-Tritsch IE et al. AJOG (2012)

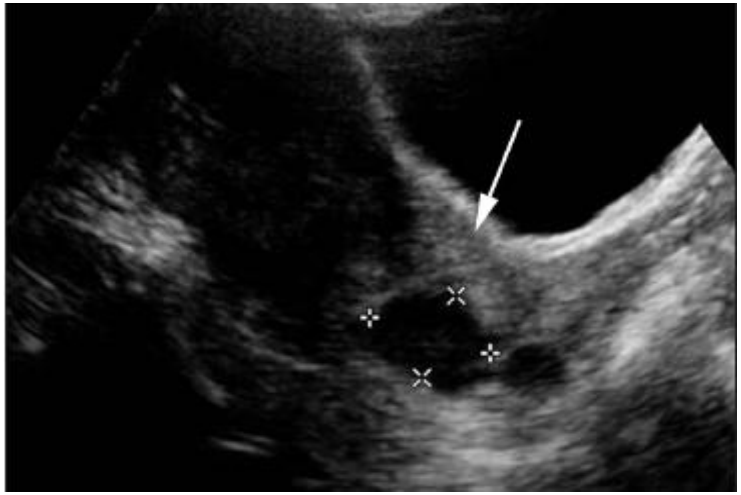
Differential Diagnosis

Miscarriage in progress



- Lack of color flow
- Positive “sliding-sign”
- Short-interval follow-up

Cervical ectopic pregnancy



- Centered in the cervical canal
- Normal thickness of anterior myo

Osborn DA et al. J Ultrasound Med (2012)

Four main Complications

1. **Massive Hemorrhage**
2. **Uterine rupture**
3. **Higher risk of Placenta previa (accreta, increta, percreta)**
4. **Higher risk of AV-Malformations**

N=47	
12 (26%)	induced abortions leading to hemorrhage (and hysterectomy)
15 (32%)	(spontaneous) uterine rupture – most of them silent
8 (17%)	AV-malformation
37 (79%)	Laparotomy
35 (74%)	Hysterectomy
47 (100%)	Defects in placentation **in ALL!!!**

Timor-Tritsch IA & Monteagudo A AJOG (2012)

CSP Treatment – High Complication Rate

First-line treatment choices for cesarean scar pregnancy with the most and the least complication rates

Treatment alone or in combination	Cases, n	Complications, n	%
MTX alone	87	54	62.1
D&C[a]	305	189	61.9
UA embolization[a]	64	30	46.9
Hysteroscopy[a]	119	22	18.4
Local intragestational injection of MTX/KCL (TAS or TVS guidance)[a]	81	8	9.6

D&C, dilation and curettage; *KCl,* kalium chloride; *MTX,* methotrexate; *TAS,* transabdominal; *TVS,* transvaginal; *UA,* uterine artery.

[a] Alone or in any combination.

Timor-Tritsch. Early placenta accreta and cesarean section scar pregnancy: a review. Am J Obstet Gynecol 2012.

Timor-Tritsch IA & Monteagudo A AJOG (2012)

Treatment Options

- "The main difficulty in counseling women diagnosed with asymptomatic scar pregnancy is our lack of understanding of the natural history of the condition and our inability to predict the likelihood of different outcomes."

Early versus Late treatment

N=184 divided in two groups

(1) good outcome (no complication & elective intervention w/o complication)
(2) Complication group (emergency surgery, embolization required)

Clinical outcome of patients with CSP as a function of gestational age at first treatment

	Gestational age, wks				
Outcome[a]	5-6	7	8	9	10-15
No complications	51	35	14	4	4
Complications	12	16	26	6	16

CSP, cesarean section scar pregnancy.

Timor-Tritsch IA & Monteagudo A AJOG (2012)

Exspectant Management

TYPE-1: Implantation on top of the scar, progression towards uterin cavity (viability achievable, **risk of bleeding high)**

Few cases with progression of pregnancy near term and life birth - POSITIVE

1. **Herman A et al. BJOG (1995)** – uterine rupture in 35. gw, CD w/o Hysterectomy
2. **Bai XX et al. Cin Med J (2012)** – heterotopic CSP with intrauterine abortion and uneventful term at 36 gw

- 44% of CSP terminate in spontanous miscarriage (surgical treatment in 29%)[1]
- 4/4 cases of CSP termination at 20 gw due to uterine rupture[2]
- 3/3 hysterectomies in 15, 17 & 21 gw due to massive hemorrhage[3]

[1]Sadeghi H et al. Am J Perinat (2010),[2]Jurkovic D et al. UOG (2012),
[3]Timor-Tritsch IE et al. AJOG (2012)

Dilatation & Curettage (D&G)

CAVE: trophoblastic tissue outside the uterine cavity and not reachable

N=21	
5 (24%)	No complication
16 (76%)	additional treatment due to complication (3 hysterectomies, laparotomy and excision, systemic MTX)

Rotas MA et al. Obstet Gynecol (2006)

Experience of D&C due to incorrect diagnosis of CSP
80% severe hemorrhage (3 hysterectomies due hypovolaemic shock)

Zhang Y et al. JOGR (2013)

4 cases of early CSP successfully treated by **suction curetage**

Patient no.	Age (years)	No. of prior cesarean section(s)	Missing period (weeks)	β-hCG (mU/mL) (before suction)	Gestational sac (mm) diameter	Myometrial thickness (mm)
1	30	1	5	1,681	10	6.9
2	38	3	6	7,362	11.4	5.8
3	29	3	6.4	7,726	24	4.7
4	37	2	7	15,573	14	6.3

Tekin YB et al. Arch Gynecol Obstet (2014)

Medical Treatment

appropriate patient: **pain free**, **hemodynamic stable**, **unruptured CSP**, **RMT < 2mm**

Systemic MTX

- Typically 50mg/m² i.m.
- Ideal in small CSPs – HCG < 10,000 mIE/mL; GS ≤ 10mm; ≤ 9 gw
- Success rate 71-80%[1]
- **Fibrous tissue around GS can delay drug absorbance**
- **Short half-life of MTX**
- **Multiple doses required**[2]

N=16
5 (31%) – HCG < 5,000 mIE/mL … 1 application successful
5 (31%) – multiple doses required … success in 3; Hysterectomy in 2
6 (38%) – HCG 6,000 – 48,000 mIE/mL … **additional treatment**

Rotas MA et al. Obstet Gynecol (2006)

[1]Ash A et al. BJOG (2007); [2]Li N et al. UMB (2012)

Medical Treatment

Addition of local MTX

- Retrospective series of 26 pts. (6-14 gw; 1x CD 15; 2x CD 9; 3x CD 2)
- 12 pts. from other sites with prior systemic MTX **(11/12 with positive FHR!)**

Measure	Mean
hCG, mIU/mL	4334.6
Volume, mL	18.1
VI	18.9

25mg MTX (1mL) into GS
25mg MTX outside GS
25mg MTX i.m.

60-90 min confirmation of negative FHR
Follow-up scan 24-48 hrs. later

19 pts. treated by L & S MTX

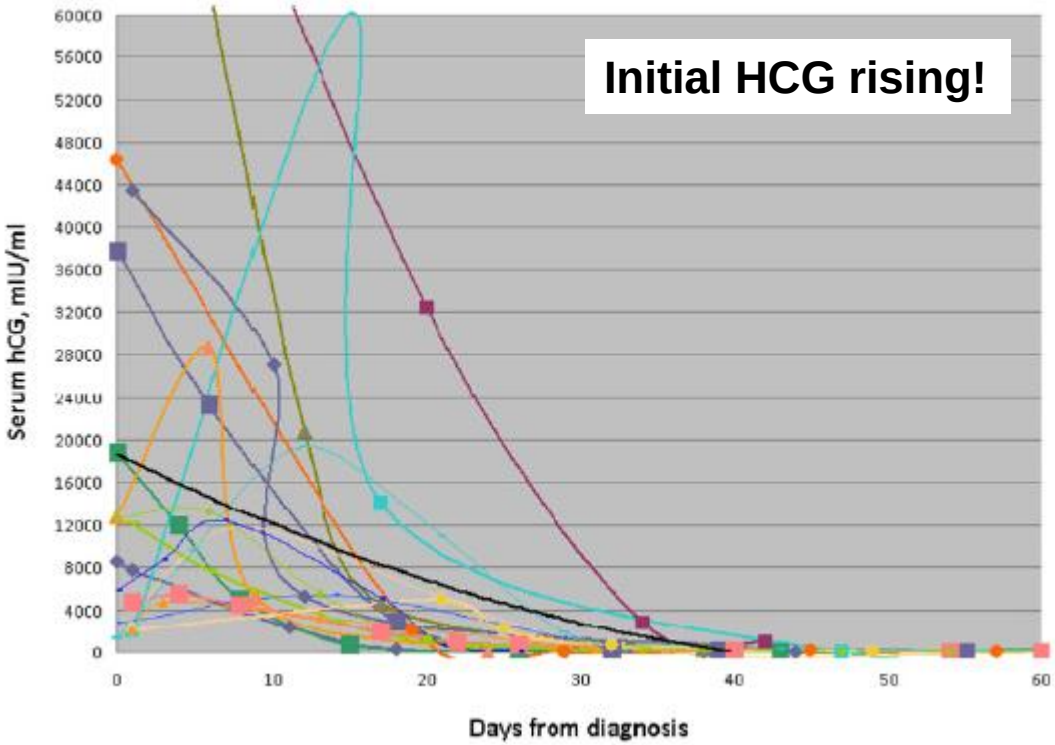
No complications
Mean time of resolution 88 days

7 pts. w/o treatment

2 refused treatment – TAH
2 hemorrhage due to AV-malf. – TAH
3 no FHR – resolved spontaneously

Timor-Tritsch IE et al. AJOG (2014)

Medical Treatment



3 Follow-up Parameters

A) Serial serum HCG
B) Volume of GS
C) Degree of vascularization

CAVE: Late complications in HCG droppers & negatives possible!

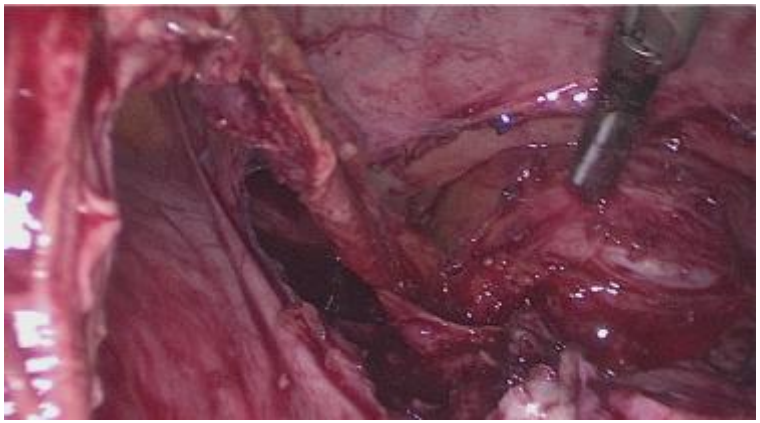
Timor-Tritsch IE et al. AJOG (2014)

Surgical Treatment

In case of complication & emergency – Hysterectomy (TAH)

Excision of CSP / scar via LSK or Lap

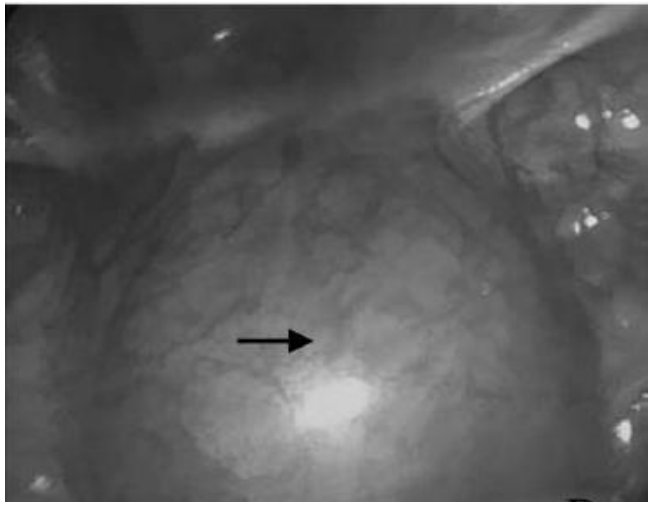
- Quick dropping of HCG
- shorter follow-up
- Excision of scar is possible
- Preservation of uterus (fertility)



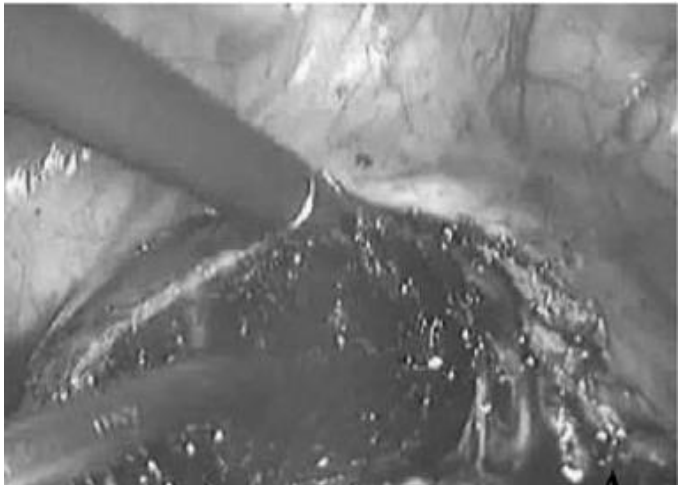
N = 6 (LSK approach)
Median time 61.5 min
Median Blood loss 83.5 ml
Laparoscopic instillation of vasopressin
Prior MTX application

Zhang Y Gyn Obstet Invest (2013)

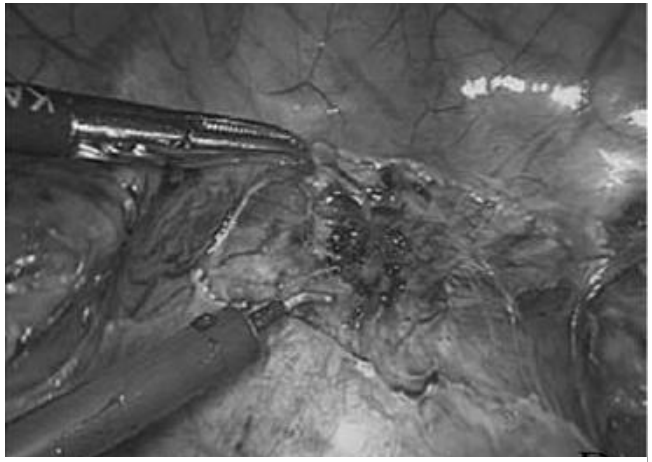
LSK Approach



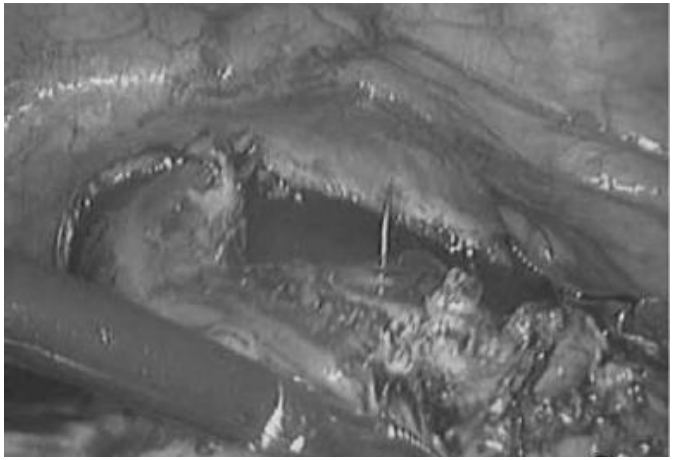
Bulging mass in low uterine segment



Uterus wall opened, GS suction



Thin myometrial layer after incision



One layer suture

Wang HY et al. JSLS (2013)

LSK Approach

N = 11 (CSP after 1 CD (9) or 2 CD (2))

HCG 2,100 – 74,000 mIE/mL
Small GS; 5-9 gw

- LSK successfully in 11/11
- First Step was LSK Ligation of UA in all pts.
- Median surgical time 85 min
- Median blood loss 250 ml
- HCG levels return < 100 mIE/mL after (median) 16.4 days

Wang HY et al. JSLS (2013)

Vaginal Approach

N = 31 (divided in 3 groups)

(A) Excision of CSP & uterine wall repair (11 pts.)
(B) transvaginal ligation of UA followed by D&C (7 pts.)
(C) Resection of anterior uterine wall & repair (9 pts.)

- Higher blood-loss when uterine wall resected
- No bladder injury; Uterus preserved in all cases
- Median surgical time 40 min (no diff. in groups)
- HCG levels recovery (median) 2.8 weeks (no diff. in groups)

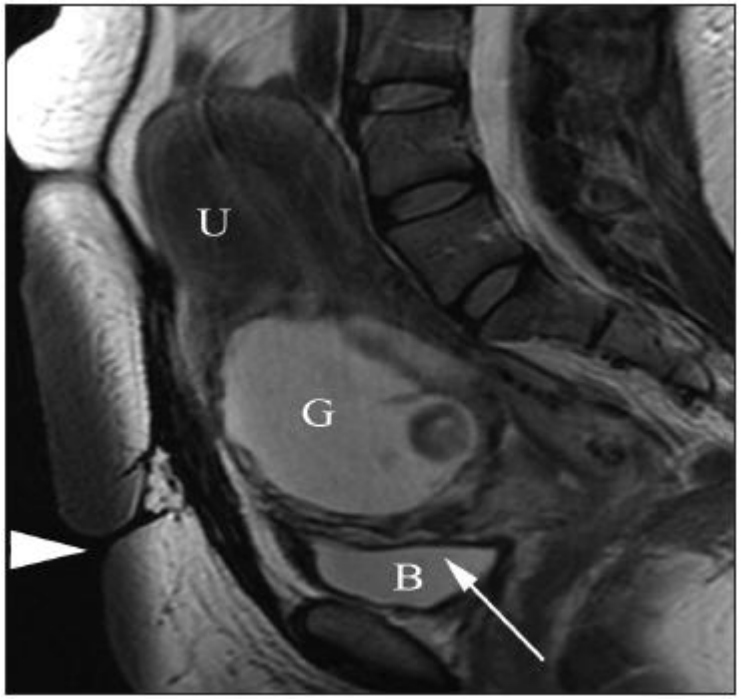
Lu HY et al. Zonh Hua (2011)

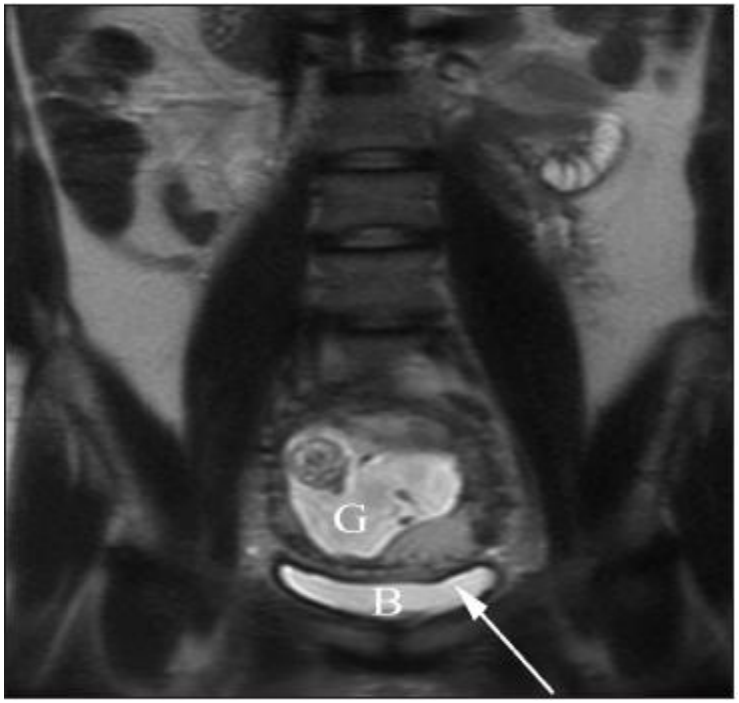

Vielen Dank …!

Diagnosis of Cesarean Scar Pregenancy

Magnetic Resonance Imaging

- Better evaluation of pelvic anatomy
- Intraoperative orientation
- Possible bladder involvement
- Measurement of lesion volume – prediction of MTX success





Osborn DA et al. J Ultrasound Med (2012)