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 pregnancy – CSP”
- “cesarean ectopic pregnancy”
- “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\textsuperscript{1}
• 112 cases up to 2002\textsuperscript{2}
• 751 cases up to 2012\textsuperscript{3}

Is CSP real ectopic?

Since no official definition agreement ...

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**)

Incidence

Incidence ranging from $1:1,800 - 1:2,216^1$
~ 6.1% of ectopic pregnancies (with history of CD)$^1$

cervical pregnancy 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%)

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)

STATISTIK AUT 2013
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 pregnancies (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
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)

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

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<table>
<thead>
<tr>
<th>Indication</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breech presentation</td>
<td>11</td>
<td>31.4</td>
</tr>
<tr>
<td>Fetal distress</td>
<td>8</td>
<td>22.9</td>
</tr>
<tr>
<td>Arrest of labor</td>
<td>7</td>
<td>20</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>4</td>
<td>11.4</td>
</tr>
<tr>
<td>Placenta previa</td>
<td>3</td>
<td>8.6</td>
</tr>
<tr>
<td>Twin gestation</td>
<td>2</td>
<td>5.7</td>
</tr>
</tbody>
</table>

Undeveloped lower uterine segment in case of Breech presentation?
**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 Chaillot, PhD; Lynne Moore, PhD; Emmanuel Bujold, MD, MSc

Systematic Rev. + Meta-Analysis (N=20 (6 of them randomized trials)
### 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 Chaillot, PhD; Lynne Moore, PhD; Emmanuel Bujold, MD, MSc

#### TABLE 2

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. of trials</th>
<th>No. of participants</th>
<th>Prevalence</th>
<th>RR (95% CI)</th>
<th>P value</th>
<th>I²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Single layer (%)</td>
<td>Double layer (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal infectious morbidity</td>
<td>10</td>
<td>5868</td>
<td>416/2937 (14.2)</td>
<td>425/2931 (14.5)</td>
<td>0.92 (0.74–1.15)</td>
<td>.48</td>
</tr>
<tr>
<td>Endometritis</td>
<td>8</td>
<td>13,815</td>
<td>196/6907 (2.8)</td>
<td>183/6908 (2.6)</td>
<td>1.04 (0.81–1.34)</td>
<td>.76</td>
</tr>
<tr>
<td>Wound infection</td>
<td>8</td>
<td>13,730</td>
<td>566/6856 (8.3)</td>
<td>612/6874 (8.9)</td>
<td>0.93 (0.83–1.04)</td>
<td>.18</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>7</td>
<td>14,313</td>
<td>141/7149 (2.0)</td>
<td>164/7164 (2.3)</td>
<td>0.86 (0.69–1.08)</td>
<td>.19</td>
</tr>
</tbody>
</table>

**Means**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. of trials</th>
<th>No. of participants</th>
<th>Mean difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean blood loss, mL</td>
<td>6</td>
<td>1025</td>
<td>−40 (−110 to 29)</td>
</tr>
<tr>
<td>Duration of cesarean, min</td>
<td>9</td>
<td>4722</td>
<td>−6.1 (−8.7 to −3.4)</td>
</tr>
<tr>
<td>Hospital stay, d</td>
<td>5</td>
<td>4063</td>
<td>−0.3 (−0.7 to 0.0)</td>
</tr>
</tbody>
</table>

CI, confidence interval; RR, risk ratio.

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)

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

**TABLE 3**

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

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. of trials</th>
<th>No. of participants</th>
<th>Prevalence</th>
<th>RR (95% CI)</th>
<th>P value</th>
<th>I^2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scar defect evaluated by US</td>
<td>3</td>
<td>193</td>
<td>25/100 (25.0)</td>
<td>0.53 (0.24–1.17)</td>
<td>.12</td>
<td>67%</td>
</tr>
<tr>
<td>Uterine rupture or dehiscence</td>
<td>2</td>
<td>187</td>
<td>4/83 (4.8)</td>
<td>2.38 (0.63–8.96)</td>
<td>.20</td>
<td>0%</td>
</tr>
</tbody>
</table>

**Means**

<table>
<thead>
<tr>
<th>LUS thickness, mm</th>
<th>No. of trials</th>
<th>Participants</th>
<th>Mean</th>
<th>Mean difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15.0</td>
<td>2</td>
<td>240</td>
<td>17.6</td>
<td>−2.6 mm (−3.1 to −2.2)</td>
</tr>
</tbody>
</table>

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


Double-layer = myo thickness increase
**Locked vs. Unlocked**

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

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

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“… 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 blood²

Diagnosis of uterine scar defects (I)

36y; IG/IP, 1x CD, perimenstrual spotting
Diagnosis of uterine scar defects (II)

Detection via TVS, KM-Hysteroscopy, Hysteroscopy

A … craniocaudal length of scar
B … depth of scar
C … width of scar (vertical)
D … RMT (residual myometrial thickness)
Diagnosis of uterine scar defects (III)

A … craniocaudal length of scar
B … depth of scar
D … RMT (residual myometrial thickness)
Diagnosis of Cesarean Scar Pregenancy

<table>
<thead>
<tr>
<th>Presenting Symptom</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>21</td>
<td>36.8</td>
</tr>
<tr>
<td>Painless vaginal bleeding</td>
<td>22</td>
<td>38.6</td>
</tr>
<tr>
<td>Abdominal pain and bleeding</td>
<td>9</td>
<td>15.8</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>5</td>
<td>8.8</td>
</tr>
</tbody>
</table>


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))

Diagnosis of Cesarean Scar Pregnancy

Sensitivity (first trimester) – 86.4\%^{1}

Diagnosis of Cesarean Scar Pregnancy

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
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!!! |
## CSP Treatment – High Complication Rate

<table>
<thead>
<tr>
<th>Treatment alone or in combination</th>
<th>Cases, n</th>
<th>Complications, n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTX alone</td>
<td>87</td>
<td>54</td>
<td>62.1</td>
</tr>
<tr>
<td>D&amp;C$^a$</td>
<td>305</td>
<td>189</td>
<td>61.9</td>
</tr>
<tr>
<td>UA embolization$^a$</td>
<td>64</td>
<td>30</td>
<td>46.9</td>
</tr>
<tr>
<td>Hysteroscopy$^a$</td>
<td>119</td>
<td>22</td>
<td>18.4</td>
</tr>
<tr>
<td>Local intragestational injection of MTX/KCL (TAS or TVS guidance)$^a$</td>
<td>81</td>
<td>8</td>
<td>9.6</td>
</tr>
</tbody>
</table>

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

$^a$ Alone or in any combination.

• “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

<table>
<thead>
<tr>
<th>Outcomea</th>
<th>Gestational age, wks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5-6</td>
</tr>
<tr>
<td>No complications</td>
<td>51</td>
</tr>
<tr>
<td>Complications</td>
<td>12</td>
</tr>
</tbody>
</table>

CSP, cesarean section scar pregnancy.
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


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

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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) |

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

4 cases of early CSP successfully treated by suction curetage

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


Zhang Y et al. JOGR (2013)

Tekin YB et al. Arch Gynecol Obstet (2014)
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

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<table>
<thead>
<tr>
<th>N=16</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 (31%) – HCG &lt; 5,000 mIE/mL … 1 application successful</td>
</tr>
<tr>
<td>5 (31%) – multiple doses required … success in 3; Hysterectomy in 2</td>
</tr>
<tr>
<td>6 (38%) – HCG 6,000 – 48,000 mIE/mL … <strong>additional treatment</strong></td>
</tr>
</tbody>
</table>

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!)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>hCG, mIU/mL</td>
<td>4334.6</td>
</tr>
<tr>
<td>Volume, mL</td>
<td>18.1</td>
</tr>
<tr>
<td>VI</td>
<td>18.9</td>
</tr>
</tbody>
</table>

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-Trisch 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!
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
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)
Vielen Dank ...!
Diagnosis of Cesarean Scar Pregnancy

Magnetic Resonance Imaging

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