Ultrasound markers of pre-eclampsia

G. Macé, E. Cynober, B. Carbonne

Hôpital Saint-Antoine, Paris

Placental disease
Abnormal trophoblastic invasion

Endothelial activation

Placental ischemia

Vasoconstriction / micro-thromboses

majoration of ischemia

Maternal endothelial activation

Pre-eclampsia

HELLP syndrome

IUGR

abruption

stillbirth
Ultrasound markers

- Uterine Dopplers
- Fetal growth
- Fetal Dopplers

\[ PI = \frac{S-D}{m} \quad \text{RI} = \frac{S-D}{S} \text{ or DI=D/S} \]
Insufficient colonization  normal colonization

A, C, D and B

B/A: Diastolic Index
A-B/A: Resistance Index
A-B/m: Pulsatility Index

« The Notch »
Technical aspects of measurement

Transabdominal Pseudo-crossing

Transvaginal Uterine crossing

Transversal view

Para sagittal right UA

Para sagittal left UA
Slight changes: pathologic threshold

Factors altering the measurement

- Pressure on the probe
- Maternal hemodynamic fluctuations
- Level of signal on the artery
- Uterine contractions
Abdominal pressure

Factors influencing the notching

• Maternal heart rate
• Decreased speed: spread intervals
Amplitude
Change probe axis: parallel to the artery
Differential diagnosis

arcuate artery

Diagnosis of notching

- Adequate artery at the adequate level
- Significant if permanent
- Increased RI frequently associated
- Evolution during pregnancy
  = Clinical impact
reference curves for PI
first trimester, and until term

Chagnaud et al 2008  Gomes et al 2008

Evolution of notching

Gomes et al, 2008
Choice of indices (*Cnossen CMAJ 2008*)
Meta-analysis, 74 studies, n= 79547

Maternal risk factors for preeclampsia

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>LR+</th>
</tr>
</thead>
<tbody>
<tr>
<td>African</td>
<td>1.45</td>
</tr>
<tr>
<td>BMI ≥ 35</td>
<td>2.18</td>
</tr>
<tr>
<td>Chronic HTA</td>
<td>12.52</td>
</tr>
<tr>
<td>Personal history PE</td>
<td>3.19</td>
</tr>
<tr>
<td>Nullipara</td>
<td>1.23</td>
</tr>
<tr>
<td>Parity ≥ 2</td>
<td>1.72</td>
</tr>
</tbody>
</table>

Define standard high risk population

*Papagiorghiou 2005*
Maternal risk factors for preeclampsia

<table>
<thead>
<tr>
<th>Factor</th>
<th>LR+</th>
</tr>
</thead>
<tbody>
<tr>
<td>African</td>
<td>1.45</td>
</tr>
<tr>
<td>BMI $\geq 35$</td>
<td>2.18</td>
</tr>
<tr>
<td>Chronic HTA</td>
<td>12.52</td>
</tr>
<tr>
<td>Personal history PE</td>
<td>3.19</td>
</tr>
<tr>
<td>Nullipara</td>
<td>1.23</td>
</tr>
<tr>
<td>Parity $\geq 2$</td>
<td>1.72</td>
</tr>
</tbody>
</table>

Prediction of PE (FP fixed 25%)

Maternal Characteristics = 45.3%
Uterine artery Doppler = 63.1%
Combination of both = 67.5%

Papagiorghiou 2005

T2 Doppler Screening

LR low risk second trimester (Cossen 2008)
### Low risk T2 Doppler

**n=1580 (Papageorghiou 2005)**

<table>
<thead>
<tr>
<th>Reference</th>
<th>SPR (%)</th>
<th>Spec (%)</th>
<th>Sens (%)</th>
<th>Prev (%)</th>
<th>PPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steal et al15</td>
<td>11.6</td>
<td>89</td>
<td>63</td>
<td>1.9</td>
<td>2.35</td>
</tr>
<tr>
<td>Bonfay et al16</td>
<td>5.6</td>
<td>95</td>
<td>95</td>
<td>4.6</td>
<td>12.99</td>
</tr>
<tr>
<td>Bower et al17</td>
<td>16.0</td>
<td>86</td>
<td>75</td>
<td>2.3</td>
<td>3.51</td>
</tr>
<tr>
<td>Valentin et al18</td>
<td>9.6</td>
<td>93</td>
<td>89</td>
<td>3.3</td>
<td>4.62</td>
</tr>
<tr>
<td>North et al19</td>
<td>11.9</td>
<td>89</td>
<td>77</td>
<td>3.4</td>
<td>5.71</td>
</tr>
<tr>
<td>Harrington et al20</td>
<td>9.1</td>
<td>93</td>
<td>77</td>
<td>3.7</td>
<td>6.84</td>
</tr>
<tr>
<td>Friscia et al21</td>
<td>8.6</td>
<td>92</td>
<td>50</td>
<td>1.9</td>
<td>7.63</td>
</tr>
<tr>
<td>Viron et al22</td>
<td>12.8</td>
<td>88</td>
<td>26</td>
<td>3.3</td>
<td>11.71</td>
</tr>
<tr>
<td>Kurt et al23</td>
<td>12.4</td>
<td>89</td>
<td>62</td>
<td>2.2</td>
<td>13.71</td>
</tr>
<tr>
<td>Alboga et al24</td>
<td>7.3</td>
<td>94</td>
<td>45</td>
<td>2.7</td>
<td>21.42</td>
</tr>
<tr>
<td>Aquilina et al25</td>
<td>9.8</td>
<td>93</td>
<td>60</td>
<td>5.5</td>
<td>30.18</td>
</tr>
<tr>
<td>Papageorghiou et al26</td>
<td>5.1</td>
<td>95</td>
<td>41</td>
<td>1.4</td>
<td>30.18</td>
</tr>
<tr>
<td>Pooled LR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5.90</td>
</tr>
</tbody>
</table>

Prevalence 3-5%: For FP rate 5%, 50% PE identified

### Early screening, low risk

Identifies 30% severe PE, better after 13 SA

**Likelihood Ratio for Pre-eclampsia**

- Harrington et al
- Cnossen et al
- Melchiorre et al
- Martin et al
Optimization of uterine artery Doppler, maternal history and evolution during pregnancy

Early and late PE, ROC curves. *(Plasencia, UOG 2008)*

Predictive value of Notching in a high-risk population *(Bats 2002)*

<table>
<thead>
<tr>
<th></th>
<th>1st trim.</th>
<th>2nd trim.</th>
<th>3rd trim.</th>
</tr>
</thead>
<tbody>
<tr>
<td>% notch</td>
<td>38 %</td>
<td>19 %</td>
<td>18 %</td>
</tr>
<tr>
<td>PPV</td>
<td>50 %</td>
<td>50 %</td>
<td>40 %</td>
</tr>
<tr>
<td>NPV</td>
<td>92 %</td>
<td>91 %</td>
<td>81 %</td>
</tr>
<tr>
<td>Sens.</td>
<td>75 %</td>
<td>50 %</td>
<td>33 %</td>
</tr>
<tr>
<td>Spec.</td>
<td>75 %</td>
<td>90 %</td>
<td>85 %</td>
</tr>
</tbody>
</table>
**Treatment: Aspirin?**

**Recurrence of pre-eclampsia**

*Duley et al. BMJ 2001*

---

**Prospective Randomised trials**

Low-risk: Doppler at 20-24 SA, aspirin if pathologic

Control group: No Doppler

Outcome measure: prevalence of pre-eclampsia
Aspirin in a high risk population during first trimester

*Vainio et al 2002*

Selection on Bilateral notching at 12 weeks
Randomised Control Study
45 aspirin / 45 placebo
30 controls without notching

<table>
<thead>
<tr>
<th></th>
<th>AS (43)</th>
<th>Placebo (43)</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTA of pregnancy</td>
<td>11.6</td>
<td>37.2</td>
<td>0.31 (0.13-0.78)</td>
</tr>
<tr>
<td>PE</td>
<td>4.7</td>
<td>23.3</td>
<td>0.20 (0.05-0.86)</td>
</tr>
<tr>
<td>IUGR</td>
<td>2.3</td>
<td>7</td>
<td>0.33 (0.04-3.08)</td>
</tr>
</tbody>
</table>

- Bilateral notching T1 as screening test?
  - prevalence 55% (Martin et al)
  - Not randomised

- Clinical impact
  - Aspirin in identified groups leads to a decreasing of mild proteinuric HTA
  - Lack of power considering severe PE

⇒ Clinical benefit to prove regarding difficult ultrasound practice to generalised

*Comments on Vainio et al 2002*
low dose Aspirin in high risk population before 20 WG

![Graph showing study results with relative risks and confidence intervals](image)

_Coomarasamy RCOG 2002_

---

**Strategy for PE prediction**

<table>
<thead>
<tr>
<th>Previous obstetrical history</th>
<th>Second trimester UD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic HTA</td>
<td>LR &gt; 5, PPV &gt; 50%</td>
</tr>
<tr>
<td>Early Uterine artery doppler</td>
<td>NPV similar to low risk</td>
</tr>
<tr>
<td>in low risk?</td>
<td>Cnossen, 2008</td>
</tr>
</tbody>
</table>

Optimal surveillance but no treatment exists after 22WG → early UD in high risk / Biomarkers / algorythms?
Conclusion

- Uterin doppler is a « physiological » marker
- Effective tool if skilled operator
- Time screening dilemma
- No clinical benefit on RCT
- Associated maternal factors optimization

→ Others predictive markers?