Maternal cardiovascular profiling in the first trimester of pregnancies complicated with gestation induced hypertension or fetal growth restriction.

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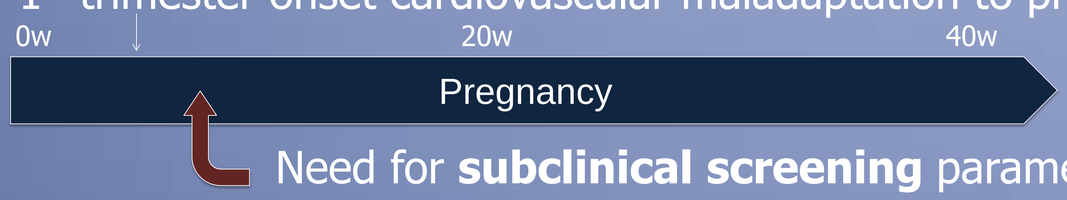
Introduction

Gestational Hypertensive Disorders (GHD)

- Pregnancy-induced hypertension with or without proteinuria
- 1st trimester onset cardiovascular maladaptation to pregnancy



Need for **subclinical screening** parameters using straightforward and reliable techniques

Objectives

To evaluate whether **maternal cardiovascular profiling** at 12 weeks of gestation (using impedance cardiography (ICG) and combined ECG Doppler ultrasonography) can **detect 1st trimester differences** between women with uncomplicated pregnancies (UP) and those who will develop **GHD** or normotensive fetal growth restriction (**FGR**).

Methods

Prospective cohort study of 242 healthy pregnant women

- Randomly selected in the 1st trimester of pregnancy at the outpatient obstetric ultrasound clinic of Ziekenhuis Oost Limburg, Genk, Belgium.
- Cardiovascular profiling at 12 weeks of gestation, using ICG and combined ECG Doppler ultrasonography, according to standardised protocols [1,2].
- Postpartum determination of clinical outcome:
  - UP (n=218)
  - GHD (n=13)
  - FGR (n=11)

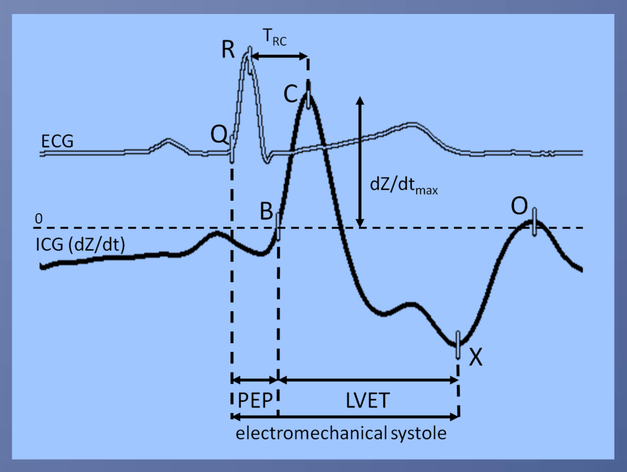


Figure I - The signals of the impedance cardiogram (ICG). ICG (dZ/dt) is the first mathematical derivative of the change in impedance over time (Z) to an alternating current with a high frequency (60–100 kHz) and a low amplitude (1 mA) transmitted through the maternal thorax by a four-electrode arrangement. Q: start of ventricular depolarization, R: peak ventricular depolarization, B: opening of the aortic valve, C: peak systolic flow (dZ/dtmax), X: closure of the aortic valve, O: opening of the mitral valve, PEP: pre-ejection period, LVET: left ventricular ejection time, and TRC: time from point R to point C.

Results & Discussion

First trimester ICG Measurements – Standing position	FGR (n = 11)	p-value	UP (n = 218)	p-value	GHD (n = 13)
Pressures					
SBP (mmHg)	114 (4.80)	0.614	115 (0.25)	**0.015**	123 (3.54)
DBP (mmHg)	76 (3.71)	0.455	76 (0.48)	**0.011**	82 (2.26)
MAP (mmHg)	86 (3.83)	0.522	86 (0.51)	**0.004**	93 (2.42)
PP (mmHg)	38 (3.24)	0.470	39 (0.63)	0.269	41 (2.09)
Left ventricular output parameters					
HR (beats/min)	95 (3.46)	0.986	96 (0.87)	0.830	94 (1.79)
SV (ml)	67 (3.97)	**0.033**	77 (1.16)	0.541	81 (5.70)
CO (ml/min)	6.2 (0.31)	**0.025**	7.3 (0.10)	0.655	7.6 (0.57)
Cardiac cycle time intervals					
PEP (ms)	95 (4.70)	0.373	98 (0.99)	0.479	100 (6.42)
PEPi (%)	15 (0.82)	0.401	15 (0.19)	0.517	16 (1.06)
LVET (ms)	249 (8.14)	0.528	244 (1.58)	0.197	251 (5.71)
LVETi (%)	39 (0.97)	0.287	38 (0.23)	0.459	39 (0.88)
DT (ms)	301 (19.33)	0.890	300 (4.38)	0.649	292 (11.18)
DTi (%)	46 (1.47)	0.996	46 (0.31)	0.306	45 (1.03)
STR	0.38 (0.02)	0.299	0.41 (0.01)	0.751	0.41 (0.03)
Thoracic fluid parameters					
TFC (1/kΩ)	23.8 (0.63)	0.169	25.1 (0.21)	0.668	25.6 (0.99)
Aortic flow parameters					
VI (1/1000/s)	71 (5.08)	0.918	71 (0.96)	**0.016**	61 (4.91)
ACI (1/100/s²)	136 (12.75)	0.892	133 (2.25)	**0.023**	106 (11.26)
HI (Ω/s²)	25.9 (1.98)	0.180	23.1 (0.35)	**0.019**	19.2 (1.70)
TAC (ml/mmHg)	1.9 (0.15)	0.215	2.1 (0.04)	0.603	2.0 (0.13)

Table I - First trimester ICG measurements in the standing position. Data are presented as means (± SEM). Differences between groups are presented as p-values (bold when significant at nominal level α = 0.05) and were calculated using Mann-Whitney U-tests. FGR: fetal growth restriction, UP: uncomplicated pregnancy, GHD: gestational hypertensive disorders, SBP: systolic blood pressure, DBP: diastolic blood pressure, MAP: mean arterial pressure, PP: pulse pressure, HR: heart rate, SV: stroke volume, CO: cardiac output, PEP: pre-ejection period, LVETi: left ventricular ejection time corrected for HR, DTi: diastolic time corrected for HR, STR: systolic time ratio, TFC: thoracic fluid content, VI: velocity index, ACI: acceleration index, HI: Heather index, TAC: total arterial compliance.

<u>UP vs GHD</u>

- Increased blood pressures
  - systolic blood pressure (SBP)
  - diastolic blood pressure (DBP)
  - mean arterial pressure (MAP)
- Decreased ICG aortic flow parameters
  - aortic velocity index (VI)
  - acceleration index (ACI)
  - Heather index (HI)

→ Lowered cardiac systolic function

<u>UP vs FGR</u>

- Decreased stroke volume (SV)
- Decreased cardiac output (CO)

No differences were found concerning the maternal veins (data not shown).

Conclusion

First trimester maternal CV function differs between women with uncomplicated pregnancies and those destined to develop GHD or FGR. Non-invasive CV profiling, using ICG and combined ECG Doppler ultrasonography, enables the identification of these differences. Consequently, cardiovascular profiling seems to be a valuable method for integrated assessment of maternal hemodynamics not only in the preclinical stages of this disease, but even in the first trimester.

[1] Tomsin K, Mesens T, Molenberghs G, Gyselaers W. Diurnal and position-induced variability of impedance cardiography measurements in healthy subjects. *Clinical physiology and functional imaging*. 2011;31(2):145-150. Epub 2010/11/27.
[2] Tomsin K, Mesens T, Molenberghs G, Gyselaers W. Venous pulse transit time in normal pregnancy and preeclampsia. *Reprod Sci*. 2012;19(4):431-436. Epub 2012/03/02