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CHARACTERISTICS OF THE MATERNAL JUGULAR VENOUS PULSE WAVEFORM BY COMBINED DOPPLER-ELECTROCARDIOGRAM ASSESSMENT

Inge Dierickx, Cécile Kremer, Liesbeth Bruckers, Chahinda Ghossein-Doha, and Wilfried Gyselaers

Original Paper

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Abstract

Standardized combined Doppler-electrocardiogram assessment was performed longitudinally at three different locations of internal jugular veins between 12 wk of gestation and 6 wk postnatally in 24 uncomplicated pregnancies. All images were classified as typical or non-typical based on the presence of the physiologic deflections A, X, H and C. Linear mixed models with random intercepts of typical images were used to investigate gestational changes in venous pulse transit time and venous impedance index. Unequivocal identification of venous pulse transit time and venous impedance index was possible in 2617 of 3798 (69%) and 2234 of 3798 (59%) images, respectively. The best identification rate (80%, 1018/1266) was at the right distal internal jugular vein. Venous pulse transit time increased with gestational age at all locations; venous impedance index decreased at the right sided internal jugular vein. Maternal jugular venous pulse waveform by combined Doppler-electrocardiogram allows unequivocal identification of A-deflection and calculation of venous pulse transit time and venous impedance index in around two-thirds of assessments, with the highest success rate at the right distal internal jugular vein. Gestational evolutions of venous pulse transit time and venous impedance index are similar to those reported at the level of renal interlobar and hepatic veins.

Key Words: Combined Doppler-electrocardiogram, Jugular venous pulse waveform, Venous pulse transit time, Venous impedance index, Pregnancy.

INTRODUCTION

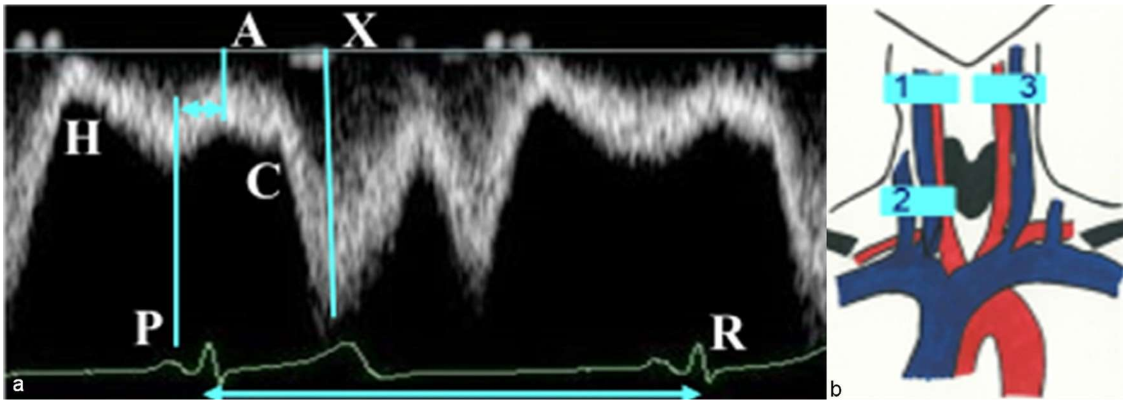
Pregnancy is characterized by multiple maternal cardiovascular changes. During the last decade, there has been increasing awareness of the potential added value of venous function assessment in better understanding maternal hemodynamics (Gyselaers and Spaanderman 2018). Combined Doppler-electrocardiogram assessment provides a safe, cheap, easily accessible and non-invasive tool to explore cerebral outflow (Dierickx et al. 2017).

Venous pulse waves indirectly reflect right cardiac atrial function and can be detected at the supracardiac and infracardiac levels (Appleton et al. 1987). The H-, A-, C- and X-deflections reflect the atrial phase of the cardiac cycle. When the atrium contracts, a retrograde wave (Doppler A-deflection) conducts into the venous system (Garg and Garg 2000). The electromechanical delay between the electrocardiogram (ECG) and the corresponding venous Doppler deflection is defined as the P-A interval. This interval is heart rate dependent and can be corrected by using the P-A interval/R-R inter- val ratio (Fig. 1a). This ratio, also referred to as the venous pulse transit time (VPT), may be considered a Doppler representative of vascular tone or wall stiffness. When the venous wall is rigid, VPT will be low as the retrograde wave will be conducted rapidly into the venous system, and the P-A interval will be shorter. On the contrary, a high VPT suggests a less rigid state of the vascular wall and can be considered a proxy for venous relaxation (Tomsin et al. 2012). The venous impedance index (VI), calculated as X-A/X, is the Doppler equivalent of the arterial resistivity index (Bateman and Cuganesan 2002) (Fig. 1a) and can be considered a proxy for distensibility and/or compliance. A large value indicates a strong intravenous rebound of atrial contraction, which counteracts venous drainage from the organs, and a decrease in VI is consistent with an increase in compliance (Gyselaers et al. 2009).

Hypertensive disorders during pregnancy are major contributors to maternal and neonatal morbidity and mortality worldwide. Numerous organs can be affected, but most deaths are attributable to cerebral dysfunction (MacKay et al. 2001). Evidence is growing that the venous heart-brain axis has an important role in the (patho)physiology of cerebrovascular hemodynamics and human brain function. If the venous outflow fails to match the arterial inflow, this will result in changes in intracranial volume and pressure (Wilson 2016; Simka and Skula 2019). To date, cerebral outflow only has been the focus of non-obstetric studies. Studying the maternal cerebrovascular volume balance with special attention to cerebral outflow is clinically relevant with respect to prediction and prevention of eclamptic insults and long-term cerebral dysfunction after pre-eclampsia/ eclampsia (Postma et al. 2014).

This study was set up to evaluate the feasibility of combined Doppler-electrocardiogram assessment of the maternal venous heart-brain axis at the level of the internal jugular veins (IJVs). For this, a reported standard pro tocol (Dierickx et al. 2017) was evaluated for acquisition of high-quality images at different IJV locations, identification of different atrial phase characteristics and evaluation of their changes throughout pregnancy.

Fig. 1. (a) Atrial phase deflections and intervals of the jugular venous pulse waveform. The H-deflection is the reflection of the rebound after passive filling of the right atrium, the A-deflection represents the intravenous rebound during the atrial contraction, the C-deflection reflects the closure of the tricuspid valve and the X-deflection is the equivalent of atrial diastole. (b) Schematic illustration of the three internal jugular vein locations: (1) right proximal, (2) right distal and (3) left proximal. ECG P-top: atrial depolarisation. ECG R top: early ventricular depolarisation



METHODS

Ethics statement

Ethics approval by the Local Ethics Committee was given before study onset (Study Reference 2011-12), and informed consent was obtained from all participants. All procedures were in accordance with institutional guidelines and adherent to the principles of the Declaration of Helsinki.

Participants

Women with apparently uncomplicated singleton pregnancies presenting in the first trimester at the outpatient antenatal clinic of Sint Lucas Hospital in Gent were invited to participate in this prospective, longitudinal cohort study. Women with pre-existing cardiac, renal, liver, hematologic or auto-immune diseases or a history of migraine or thyroid, neck or brain surgery were excluded, as were women who developed gestational complications during the observation period. Uncomplicated pregnancies were defined as those without identification of any of the criteria defined by the International Society for Studies of Hypertension in Pregnancy (ISSHP) (Brown et al. 2018) and without birth of neonates small for gestational age (SGA) according to customized sex- and parity-specific local reference charts. Repeated longitudinal measurements were performed at nine consequent points during their pregnancy (12, 16, 20, 24, 28, 32, 36 and 38 wk and 6 wk postnatally). At birth, data on gestational outcome were categorized according to the criteria revised by the ISSHP. For this study, only women with an uncomplicated pregnancy with a neonate appropriate or large for gestational age were included. Demographic details collected were maternal age (years), pregestational body mass index (BMI) as per medical history, maternal weight gain, gestational age at delivery, neonatal birth weight and birth weight percentile, smoking and medication.

Combined Doppler-electrocardiogram assessment of internal jugular veins

Combined Doppler-electrocardiogram assessment of the IJVs was performed at three different locations (right proximal, right distal and left proximal [Fig. 1b]) according to the previously described, standardized protocol with acceptable reproducibility and repeatability (equipment: Toshiba Nemio XG, 6- to 11-MHz linear- array transducer) (Dierickx et al. 2017). The importance of breath holding was explained to the participants and assessments were performed at the end of a normal expiration to minimize variation in the cross-sectional area of the target blood vessel.

At each of the nine visits, six images per location were acquired by the principal investigator. The ultrasound images, with encrypted participant details, were transferred from a portable device to the hard disk of a computer for offline assessment. IrfanView (version 64 4.41; Irfan Skiljan, Jajce, Central Bosnia Canton, Bos- nia) was used to mark and measure the flow velocities at the Doppler A- and X-deflections, the P-A interval and R-R interval (Figure 1a).

All images were classified in two categories: (i) “typical” when the Doppler A-deflection, flow velocity and associated intervals could easily be identified without guidance by the ECG and/or comparison with other patient specific simultaneously recorded images, or (ii) “non-typical” when Doppler A-wave identification was (a) possible only by ECG guidance and/or comparison with other patient-specific images or (b) not possible at all. For this analysis on physiologic changes throughout gestation, we excluded non-typical images.

The VPT and VI were calculated as (P-A)/RR and (X-A)/X for each location at each session. Linear mixed models with random intercepts to account for variation between women and to correct for dependence between different measurements from the same woman were used to investigate gestational evolutions. It was first investigated whether there was a cubic evolution. If no significant cubic effect was found, a quadratic evolution was tested and ultimately a linear evolution. Higher-order effects were not included. x^2 Tests were used to investigate associations between the presence of typical images and location. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Participants

A total of 27 women were assessed, 3 of whom were excluded: one woman with late-onset pre-eclampsia and two with SGA neonates. There were no women with fetal demise or gestational diabetes, leaving 24 participants (15 nullipara, 8 primipara and 1 multipara) eligible for inclusion. Five of the 24 women delivered between 36 and 38 wk of gestation. Patient demographics were as follows (mean ± standard deviation): maternal age, 29.6 ± 3.3 y; pregestational BMI, 22.1 ± 2.7 kg/m^2; maternal weight gain, 12.3 ± 3.7 kg; gestational age at delivery, 39.5 ± 1.2 wk; birth weight, 3348 ± 378 g; and birth weight (percentile), 51 ± 27. There were no smokers. Three women used non-cardiovascular medications (citalopram, L-thyroxine and salbutamol + budesonide inhalations).

Combined Doppler-electrocardiogram assessment of the internal jugular vein

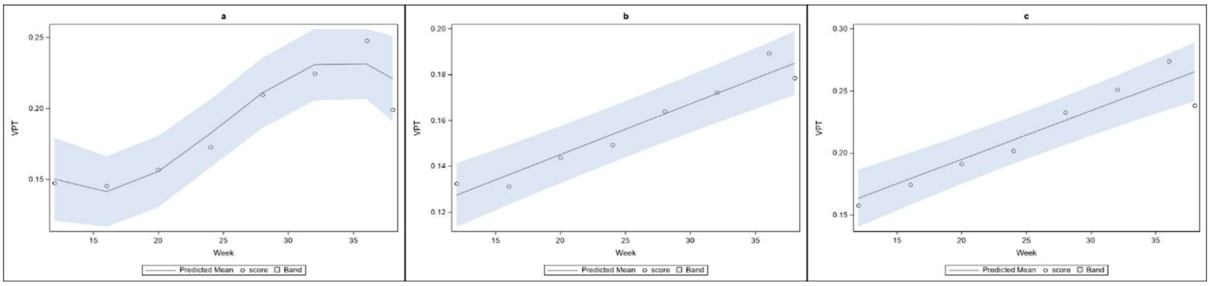
Among the total of 3798 images, typical images were found in 2617 of 3798 (69%) and 2234 of 3798 (59%) for VPT and VI, respectively (Table 1). For both VPT and VI, more typical images were found on the right-sided IJV, respectively, with odds ratios (ORs) of 2.99 (95% confidence interval [CI]: 2.59-3.46, $p \leq 0.0001$) and 2.25 (95% CI: 1.96-2.58, $p \leq 0.0001$). The odds of having a typical VPT image were 48% higher (OR = 1.48, 95% CI: 1.23-1.78, $p \leq 0.0001$) at the right distal IJV as opposed to the right proximal IJV.

Table 1. Typical and non-typical images for venous pulse transit time and venous impedance index overall and per location. Data expressed as n (%).

	Right proximal	Right distal	Left proximal	Total
	Venous pulse transit time			
Typical	931 (73)	1018 (80)	668 (53)	2617 (69)
Non-typical	335 (27)	248 (20)	598 (47)	1181 (31)
Total	1266 (100)	1266 (100)	1266 (100)	3798 (100)
	Venous impedance index			
Typical	836 (66)	820 (65)	578 (46)	2234 (59)
Non-typical	430 (34)	446 (35)	688 (54)	1564 (41)
Total	1266 (100)	1266 (100)	1266 (100)	3798 (100)

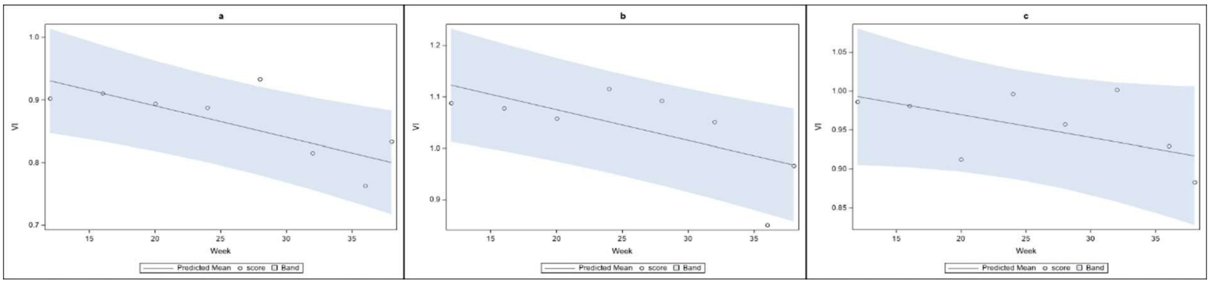
Figure 2 illustrates gestational evolutions for VPT. At the right proximal IJV, a significant cubic effect was observed with conversion from an increasing to a decreasing trend between 36 and 38 wk ($p = 0.006$). A linear increasing trend was observed at the right distal IJV and left proximal IJV from 12 to 38 wk of gestation ($p \leq 0.001$). For the three IJV locations, VPT values were significantly lower 6 wk postnatally as compared with term (right proximal: 0.139 vs. 0.198, *p* ≤ 0.001; right distal: 0.127 vs. 0.173, *p* ≤0.001; left proximal: 0.153 vs. 0.253, *p* = 0.0003) and returned to first-trimester values (right proximal: 0.139 vs. 0.131, *p* = 0.932; right distal: 0.127 vs. 0.120, *p* = 0.597; left proximal: 0.153 vs. 0.156, *p* = 0.877).

Fig. 2. Gestational evolution of venous pulse transit time (VPT) at the (a) right proximal, (b) right distal and (c) left proximal internal jugular veins. Data are illustrated as means with 95% confidence bands.



For VI, a linear decreasing trend was observed at the right proximal IJV (*p* = 0.005) and right distal IJV (*p* = 0.002) during pregnancy. VI was lower 6 wk postnatally than at a gestational age of 12 wk at the right distal IJV (0.861 vs. 1.150, *p* = 0.0047) (Fig. 3).

Fig. 3. Gestational evolution of venous impedance index (VI) at the (a) right proximal, (b) right distal and (c) left proximal internal jugular veins. Data are illustrated as means with 95% confidence bands.



DISCUSSION

Only recently are studies focusing on the role of the venous heart-brain axis in the regulation of cerebrovascular hemodynamics. To the best of our knowledge, this study is the first to focus on the jugular venous pulse waveform during uncomplicated pregnancy.

Main findings

For combined Doppler-electrocardiogram IJV assessment during uncomplicated pregnancy, three main findings were observed:

1. Unequivocal identification of VPT and VI is feasible in approximately 70% and 60% of the images, respectively. That one-third of the images were non- typical remains a weakness.
2. The success rate for obtaining high-quality images is highest at the right-sided IJV, especially the right distal IJV.
3. There is an increase in VPT and a decrease in VI at the IJVs while pregnancy advances, suggesting a decrease in vascular tone and an increase in compliance.

Strengths and limitations

This study's strengths are the large number of images, the use of customized population-specific birth weight charts, complete and directly available demographic data and the rigid standard protocol for combined Doppler-electrocardiogram IJV assessment by only one investigator. Inter-observer correlation for the assessment has previously been described as acceptable (Dierickx et al. 2017).

The present study has some limitations. First, this technique demands a highly trained investigator and is subject to both patient- and investigator-dependent artifacts. Second, intra- and inter-observer variability in identification and interpretation of the flow velocities and intervals of the jugular pulse waveform by combined Doppler-electrocardiogram assessment are not discussed in this article as they constitute the subject of a different article. Third, this study does not allow us to draw conclusions on the possibility of variables interfering within the complex functioning of cerebral outflow as reflected in the maternal jugular venous waveform.

Interpretation

The presence of about one-third non-typical combined Doppler-electrocardiogram IJV images remains a weakness. This study confirms that Doppler patterns of jugular waveforms vary widely among pregnant women. This can be explained by both physiological and patient-related factors.

First, the cerebral outflow is characterized by anatomic variants, anastomoses, valves and collateral veins. The IJVs are highly deformable and much more subject to respiration, body position and movements compared with the arterial heart-brain axis (Gisolf et al. 2004; Marcotti et al. 2015; Toro et al. 2015; Zamboni et al. 2012). Even minimal changes in intrapulmonary pressure may already interfere with supracardiac venous return and with the jugular pulse waveform.

Second, the polarity and flow velocity of the Doppler A-deflection vary widely among healthy individuals (Staelens et al. 2014), and there is an increased turbulent jugular blood flow during pregnancy (Lin et al. 2009). The retrograde pulse wave from atrial contraction is transported directly into the venous system (no valve between right atrium and venae cavae) and is then gradually extinguished with increasing distance from the heart (Downey 2005). The very short distance between the right atrium and IJVs may partly explain the large number of non-typical combined Doppler-electrocardiogram images.

Third, the valves, located distally in the IJV, are mechanically the only structures between the right atrium and the brain (Toro et al. 2015). To date, knowledge of their function remains limited; however, it seems likely that they may interfere with the retrograde propagation of the pulse waveform into the venous tree.

The aforementioned factors explain the wide variability and 30% failure of VPT and VI identification in jugular waveform patterns obtained by combined Doppler-electrocardiogram.

The right-sided IJV, especially right distal IJV, seems to be the location of preference for combined Doppler-electrocardiogram assessments. The right distal IJV is the nearest location to the body axis of a right-handed investigator, and the probe steering hand can be rested on an anatomical stabilizer, the clavicle, during the procedure (Dierickx et al. 2017). This may explain why the right proximal and left proximal IJVs seem more susceptible to the investigator's motion artifacts, variability in the probe's pressure on the skin and its angle relative to the scanning surface.

Unintentionally contralateral rotation of the women's head during the procedure might interfere with jugular blood flow. As the angle of rotation is greater at the proximal than the distal IJV, interference with the pulse waveform might be more pronounced at the proximal IJV levels (Farina et al. 2013).

Although waveforms at the thoracic inlet veins have been described as nearly bilaterally symmetric, slightly more turbulent flow typically has been observed in left-sided veins (Nazarian and Foshager 1995). This is probably due to the repetitive external compression by the pulsating aorta on the wall of the left brachiocephalic vein that is transported in retrograde direction up to the left IJV (Garg and Garg 2000). Next to that, the right-sided IJV is in a relatively direct line cephalad to the superior caval vein in contrast to the left side, where cerebral outflow is an angled line.

The investigator- and patient-dependent factors described above explain why there are fewer unequivocal Doppler waveform identifications at left-sided IJVs. This is also in line with the previous study in which concordance correlation coefficients for both intra- and inter-rater agreement in performing the combined Doppler-electrocardiogram IJV technique proved to be higher at the right-sided IJV (Dierickx et al. 2017).

Gestational changes of VPT and VI

Based on the data described in this article, we can conclude that VPT increases at both the right and left IJVs, and VI decreases at the right IJV during an uncomplicated pregnancy.

These findings agree with previous Doppler ultrasonography studies at the infracardiac level, which indicated that with gestational age, there is (i) an increase in hepatic and renal venous relaxation (higher value of VPT) and (ii) a flattening of the pulse waveform (decrease in VI), suggesting an increase in compliance (Gyselaers et al. 2008). The absence of a significant trend in VI for left-sided IJVs can be explained by the small number of unequivocal assessments (Table 1) and their wide variability (Fig. 3c) at this location.

After delivery, the IJV VPT returns to first-trimester values in the first 6 wk after delivery. This is in concordance with other studies describing venous changes at the lower extremities returning to non-pregnant values in the first postnatal months (Skudder et al. 1990).

Combined Doppler-electrocardiography of IJVs is proven to be a useful imaging modality to explore gestational changes at the venous heart-brain axis. This article is an invitation to further investigate how anatomical variations, valves and collateral veins may interact with the counteractive force of atrial systole and whether they interfere or deform the maternal jugular pulse waveform.

CONCLUSIONS

Combined Doppler-electrocardiography of IJVs is feasible in uncomplicated pregnancies. Non-typical presentation of jugular waveform characteristics remains a weakness of this methodology. The right-sided IJV is the location of preference. Changes in VPT and VI at IJVs exhibit patterns similar to those reported at the infracardiac level, suggesting a gradual increase in vascular compliance and reduction of vascular tone when pregnancy advances.