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Reproducibility and repeatability of Doppler assessment of maternal venous hemodynamics at the level of renal interlobar and hepatic veins

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Introduction

Renal vascular studies can be performed using ultrasound and duplex color flow. No significant changes in renal arterial Doppler flow have been observed (1,2), but Doppler flow of the interlobar renal veins was reported to change markedly during pregnancy (3,4).

Compared to non – pregnant women, the renal interlobar vein venous impedance index (RIVI) was lower in pregnant indivuals, and this effect was more pronounced in the third than in the second trimester (3,4). The RIVI was also higher in preëclampsia than in uncomplicated pregnancies (4,5).

Hepatic vein (HV) Doppler waveforms also change significantly during pregnancy (6). A spectrum of venous HV Doppler waveforms has been observed in the course of both uneventful pregnancies and those complicated with preeclampsia (6,9,10). Characteristics of normal HV Doppler waveforms (A,X,V and Y) resemble those observed at the inferior Vena Cava level and relate to the cardiac-cycle dependent changes of the right atrium (8).

Despite this potential clinical application, there is a lack of data in the literature on the reproducibility and repeatability of ~~doppler~~ Doppler resistance and velocimetry measurements of renal interlobar veins and hepatic veins.

The aim of this study was to assess intra- and interobserver variability of Doppler flow velocity measurements of renal and hepatic veins in pregnancy.

Patients and methods

Ultrasound examination

Before study set up, approval of the local ethical committee was obtained. In this study, the reproducibility and repeatability of our methodology was evaluated in pregnant women, attending the outpatient antenatal clinic for a routine obstetrical ultrasound scan during first, second or third trimester. After informed consent, a Doppler flow examination of the renal and hepatic veins was performed. All measurements were done by 1 of 2 sonographers or both (TM and/ or WG), using a 3.5-7 MHz probe (Hitachi EUB 6500). All women were examined in supine position at random occasions throughout the day, irrespective of food intake.

First, both kidneys were scanned in the transverse plane, after which the interlobar arteries and veins were identified using color Doppler flow mapping. The impact of breathing movements and the relevance of holding breath during measurements was explained to each patient. Once the patient was familiar with the instructions of the sonographer, the examination was performed according to a standard protocol. (1) A simultaneous Doppler signal of both interlobar arteries and veins was required for unequivocal identification of the examined vessels. (2) The real time ultrasound image in combined B-D mode was frozen after visualisation of at least 2-3 similar Doppler flow patterns during interrupted breathing. (3) The direction of the Doppler beam was adjusted according to the axis of the examined vessel when necessary, with a maximum of 30°. (4) Venous peak velocity and presystolic velocity (PSV) were plotted and VI was calculated automatically (PV-PSV/PV). (5) For every woman, six consecutive measurements were performed for each kidney and the means of three consecutive measurements were registered (10).

After this, the right, middle and left branch of the hepatovenous tree were identified using colour Doppler flow mapping, and differentiated from hepatic arteries and the portal system.

The examinations were also performed according to a standard protocol. (1) Doppler signals were sampled at three different locations from the craniocaudal midportion in the liver, preferable one sample in each of the main branches. (2) The real-time ultrasound image in combined B-D mode was frozen after visualisation of at least two to three similar Doppler flow patterns during interrrupted breathing. (3) As the direction of the Doppler beam was mostly in line with the examined vessel, adjustment was rarely necessary. If so, the axis of adjustment was always within 30°. (4)Velocities of the HV-Doppler wave characteristics A,X,V and Y were measured. For the monophasic Doppler waveforms, where Dopplerwave characteristics could not be identified, venous maximum velocity (MxV) and minimum velocity (MnV) were considered to represent the equivalents of X&Y and A&V respectively. (5) For each woman 6 measurements were performed and printed. After scanning, mean values of 3 consecutive measured values of A,X, V and Y velocities were calculated and registered in the database.

Statistical analysis

All registered values were categorized into 3 groups;~~,~~ A) 24 women evaluated twice by sonographer 1;~~,~~ B) 24 women evaluate twice by sonographer 2; and C) 24 women evaluated twice by both ultrasonographers. Intra-observer correlations were calculated in group A and B and inter-observer correlation in group C. Intra- and interobserver correlations for (1) RIV maxV, minV, RIVI and (2) HV, A, X, Y and V were computed from a linear mixed model using restricted maximum likelihood estimation (SAS procedure NLMixed) (ref Geert Molenberghs).

Ik zou hier toevoegen:

Verbeke G, Molenberghs G (2000) Linear Mixed Models for Longitudinal Data. New York: Springer.

Molenberghs G, Verbeke G (2005) Models for Discrete Longitudinal Data. New York: Springer.

For the intra-observer intraclass correlation, a compound-symmetry structure was assumed among the six measurements of the same parameter. Based on the corresponding variance components, an expression was derived for the correlation between the average of three measurements and the average of a replicate set of three measurements, in line with clinical practice.

Let tThe patient-specific random intercept has gothave variance d and t. The measurement error variance is σ^2. The intra-observer correlation follows as: $\rho = d/ (d +\sigma^2/3)$.

The inter-observer correlation is calculated similarly. Here, the variance error is $\sigma^2(00)$ for sonographer 1 and $\sigma^2(11)$ for sonographer 2. There is a random patient effect with variance d(00), with an additional effect for the random patient by rater interaction, with variance d(11). The covariance between both is d(01). The interobserver correlation between the average of three measurements of both sonographers can be calculated as follows :

$\rho = (d(00) +d(01))/ \text{sqrt}(d(00) +\sigma^2(00)/3) / \text{sqrt}(d(00) + d(11) +2d(01) + \sigma^2(00)/3 + \sigma^2(1)/3)$

The repeatability coefficient (RptC) was calculated for two consecutive measurements, performed by one sonographer in women of group (1) or (2). RptC is defined by the British Standards Institution as $2S_d$. Assuming a normal distribution, it is expected that 95% of differences between two consecutive measurements are less than two standard deviations. The 95% Confidence Interval (CI) of differences between two measurements represents the range of variation. If RptC is not within the 95% CI, there is a significant systematic difference.

When a method has a poor repeatability and RptC is high, the agreement between the measurements of two sosnographers is bound to be poor too. To assess this, reproducibility coefficient (RpC) was calculated similar to the definition of RptC for the measurements of two ultrasonographers in women of group (3). The 95% confidence limits of the inter-sonographer differences illustrate the degree of variation around the mean. The more the sonographers tend to agree, the closer the mean will be near zero. If one sonographer measures consistently higher values than the other, the mean will be far from zero, but the confidence interval will be narrow. If the sonographers tend to disagree without a consistent pattern, the mean will be near zero but the confidence interval will be wide.

Finally, the coefficient of variation (CV) was also calculated, despite its generally accepted intrinsic disadvantages, limiting its universal application. CV is a normalized measure of dispersion, defined as the ratio of the standard deviation to the mean, by which it describes the dispersion independently of the measurement unit. The higher the CV, the greater the dispersion of the variable. A CV < 1 is considered suggestive for a good model fit.

Results

A total of 72 women were investigated, 24 by rater 1, 24 by rater 2 and 24 by both raters.

The data on intra-observer repeatability for Doppler measurements of renal interlobar and hepatic vein flow velocities are presented in table 1. All velocity measurements have an ICC ≥ 0.60, except for hepatic vein X- and Y-velocimetry by sonographer 2 where ICC = 0.53 and 0.26 respectively. For all velocity measurements, RptC is within 95% CI. The coefficient of variation (CV) is systematically higher for sonographer 2 than for sonographer 1, but all values are < 1 except for hepatic vein A-velocimetry. Doppler measurements of venous impedance, represented by the renal interlobar vein impedance index (RIVI), all show an ICC of ≥ 0.76, a CV ≤ 0.30 and a RptC within 95% CI.

The data on the inter-observer reproducibility of renal interlobar and hepatic vein Doppler flow velocimetry are shown in table 2. Measurements of RIVI show an ICC of 0.66 and 0.73 for left and right kidney, respectively, and RpC values within 95% CI. ICC of all hepatic vein velocity measurements are ≤ 0.56, except for hepatic vein A- velocity which is 0,74. All RpC values are within 95% CI. Interrater differences of all velocimetry values are ≤ ± 0.38, except for hepatic vein X-, V- and Y-velocities which are > 1. As is shown, interrater differences is 0.01 and 0.02 respectively for RIVI and the limits of agreement are narrow. They are very close to zero for all renal measurements and the hepatic A-deflection measurements, with a narrow interval for limits of agreement. Mean interrater differences for other hepatic vein velocity measurements (X-, V- and Y-deflections) are ≥ 1.38.

Discussion

Many physiologic variables are known to interfere with venous blood flow, such as cardiac contractility, respiration and body position : ortostasis and gravidity reduce venous return, whereas this temporarily increases after changing to supine position until a new steady state is reached (10). External compression from intrapelvic masses, such as the gravid uterus, may also influence venous return (3,4). Next to this, a high variation of hepatic vein Doppler wave patterns in healthy individuals has been reported, both in non-pregnant (Pedersen) as in pregnant individuals (16). Finally, Doppler velocimetry values are also subject to high intra- and interobserver variation (17). Because of all these factors, ultrasonographers have long restrained from venous Doppler velocimetry. In our former study, reproducibility of single measurements of renal interlobar vein impedance index showed low intraclass correlation coefficients ranging between 0.31 and 0.35 (12). By using the mean of three consecutive measurements as the index value per kidney, ~~more stable~~stabler figures were obtained with acceptable intra-observer repeatability (4). This study is the first to assess the intra- and interobserver correlation of Doppler measurements of maternal venous hemodynamics at the level of both renal interlobar and hepatic veins, using a reported protocol (4)(16).

Despite the fact that intra-observer correlations for measurements of both sonographers were acceptable for most parameters, interobserver correlations were≥ 0.66 only for RIVI values of both kidneys and for HV-A velocities. As such, these are the parameters that seem to be best suitable so far to use in maternal venous Doppler studies.

Reported studies on repeatability of Doppler measurements in adult kidneys have mainly addressed the renal arterial tree. Intra-observer CV of 0.10 was reported for portal vein velocimetry (20) and for renal artery velocities an ICC with an average of 0.66 (18) and a CV of ≤0.30 were reported (19). Our results in renal interlobar veins are quite comparable to the reported arterial values (Table 1).

In reported interobserver studies on renal artery Doppler velocimetry (18,19), CV was 0.08 for peak systolic and end-diastolic velocities and ICC was ≥ 0.48. Our interobserver ICC values of renal interlobar vein Doppler velocimetry are much lower than that, and this was also true for hepatic vein X- and Y- velocimetry (Table 2). Our results indicate that Doppler velocimetry of renal interlobar and hepatic veins has poor reproducibility for most parameters, apart from HV-A velocities, which show ICC≥ 0,74 despite a wide range of variation (Table 1 and 2). Next to this, Renal interlobar vein impedance index also shows high repeatability and reproducibility, indicated by ICC≥ 0,66 (Table 1 and 2). Reported resistance indexes (RI) of renal arteries showed a very low ICC (18). Contrary to this, RI of hepatic arteries showed a CV of approximately 0.04 (20).

Doppler flow examinations during pregnancy have mainly focussed the uterine arteries and fetal circulations. Intraobserver repeatability of the pulsatility index in the uterine arteries of non-pregnant women is reported to be reliable (15). Additionally, this parameter of arterial resistance also had a low coefficient of variation and high intraclass correlation coefficient, both in early (13) and in mid-gestation (14). Studies on venous waveforms in the foetal circulation are also less commonly reported than arterial studies. Van Splunder (21) reported large intervals for inter-observer limits of agreement and an average intra-observer CV of 18% for Doppler measurements in fetal umbilical veins and inferior vena cava. The reported intra- and inter-observer variability of Doppler velocimetry measurements of the fetal ductus venosus were acceptable, indicated by an ICC ≥ 0.84. However implementation in a screening setting is considered to be difficult (22, 23).

Despite the fact that our observations were obtained in small groups of women and were only ~~done~~ performed by two different observers, our results indicate that some Doppler parameters of the maternal venous compartment, in particular renal interlobar veins impedance index and hepatic vein A-velocity, can be measured in a reliable and reproducible way when a stringent

protocol is used. As such, our data illustrate the feasibility and usefulness of Duplex sonography in studies of maternal venous hemodynamics and they invite to explore its role in the assessment in normal gestational physiology or in conditions of cardiovascular maladaptation, such as preeclampsia.

Table 1: Intra-observer correlation

		Sonographer 1				Sonographer 2			
		ICC	**RptC**	**95% CI**	**CV**	**ICC**	**RptC**	**95% CI**	**CV**
LK	**MxV**	0.60	3.77	(2.34;5.19)	0.23	0.79	8.22	(5.63;10.80)	0.39
	MnV	0.60	2.53	(1.56;3.49)	0.24	0.71	5.13	(3.40;6.85)	0.46
	RIVI	0.76	0.15	(0.10;0.20)	0.16	0.83	0.25	(0.17;0.32)	0.23
RK	**MxV**	0.65	4.82	(3.07;6.56)	0.24	0.70	7.39	(4.90;9.88)	0.35
	MnV	0.63	3.83	(2.10;4.54)	0.25	0.60	4.54	(2.86;6.22)	0.40
	RIVI	0.89	0.23	(0.16;0.30)	0.24	0.82	0.31	(0.21;0.40)	0.30
HV	**A**	0.93	17.14	(12.10;22.17)	2.38	0.87	14.14	(9.93;18.34)	1.99
	X	0.62	6.74	(4.25;9.23)	0.26	0.53	4.23	(2.53;5.93)	0.28
	V	0.93	11.12	(7.85;14.39)	0.70	0.75	8.63	(5.83;11.43)	0.76
	Y	0.78	8.46	(5.72;11.20)	0.33	0.26	2.56	(0.78;4.33)	0.30

ICC: Intraclass Correlation Coefficient
RptC: Repeatability Coefficient
95% CI: 95% confidence interval
CV: Coefficient of Variation
LK: Left Kidney
RK: Right Kidney
HV: Hepatic Veins
MxV: Maximum Velocity (cm/sec)
MvV: Minimum Velocity (cm/sec)
RIVI: Renal Inter lobar Vein Impedance Index
A: A-deflection (cm/sec)
X: X-deflection (cm/sec)
V: V-deflection (cm/sec)
Y: Y-deflection (cm/sec)

Table 2: Inter-observer correlation

			Reproducibility		Interrater difference	
		ICC	**RpC**	**95% CI**	**Mean**	**Limits Agr**
LK	**MxV**	0.33	7.51	(2.72;12.3)	0.37	(-0.61;1.35)
	MnV	0.32	4.75	(1.45;7.50)	0.14	(-0.47;0.76)
	RIVI	0.66	0.19	(0.07;0.31)	0.01	(-0.01;0.04)
RK	**MxV**	0.23	9.77	(5.38;14.17)	-0.29	(-1.37;0.79)
	MnV	0.23	6.43	(3.34;9.53)	-0.27	(-1.00;0.46)
	RIVI	0.73	0.30	(0.18;0.42)	0.02	(-0.01;0.05)
HV	**A**	0.74	7.97	(1.66;14.28)	0.38	(-0.77;1.53)
	X	0.33	8.57	(2.98;14.16)	1.44	(0.31;2.57)
	V	0.56	4.19	(-3.32;11.7)	1.38	(0.49;2.27)
	Y	0.24	8.52	(3.13;13.92)	1.73	(0.62;2.83)

ICC: Intraclass Correlation Coefficient
RpC: Reproducibility Coefficient
95% CI: 95% confidence interval
Limits Agr: Limits of agreement between raters (=95% confidence interval)
LK: Left Kidney
RK: Right Kidney
HV: Hepatic Veins
MxV: Maximum Velocity (cm/sec)
MvV: Minimum Velocity (cm/sec)
RIVI: Renal Inter lobar Vein Impedance Index
A: A-deflection (cm/sec)
X: X-deflection (cm/sec)
V: V-deflection (cm/sec)
Y: Y-deflection (cm/sec)

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