ORIGINAL ARTICLE

Reproducibility of the first trimester uterine artery Doppler indices: comparing the transabdominal and the transvaginal approach

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ABSTRACT

Purpose: to assess the reproducibility of the uterine Doppler pulsatility index (UA-PI) in the first trimester using the transabdominal (TA) and the transvaginal (TV) approach.

Materials and Methods: prospective study in singleton pregnancies presenting at 11-13 weeks for routine assessment. The UA-PI was measured independently by two experienced sonographers transabdominally and transvaginally according to the ISUOG guidelines. The two techniques were evaluated with the computation of the intra-class correlation coefficients (ICC) for random effects models and the limits of agreement (LOA).

Results: 221 pregnancies were examined. Mean Ut-PI was 1.63 by TA and 1.66 by TV ultrasound scan. No significant paired differences were found between TA and TV measurements ($p>0.05$) and ICC were over 0.8 in all comparisons ($p<0.001$) among the two techniques.
The intra-observer ICC ranged from 0.87 to 0.96 and the inter-observerICC ranged from 0.82 to 0.91. ICC for intra and inter-observer variability was not influenced by maternal BMI for TA nor TV measurements. LOA between operators ranged between -0.7 and 0.7.

Conclusion: UA-PI shows moderate to good intra and inter-observer variability which is not influenced by the technique or the maternal characteristics. No significant difference was observed between the TA and TV, indicating that both techniques can be used for screening purposes.

KEY WORDS Uterine Doppler, first trimester, pre-eclampsia, screening

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Introduction

Doppler studies of the uterine vessels in the late first trimester of the pregnancy can identify women at high risk for complications related to the malfunction of the feto-placental circulation whereas the sensitivity is increased for the early onset, severe disease [1]. As a result uterine artery mean pulsatility index (UA-PI) is one of the parameters commonly used in combined models predicting maternal pre-eclampsia (PET) and fetal microsomia in conjunction with other factors such as maternal weight, race, blood pressure and biochemical indices [2-7]. Although the applicability of the proposed models in populations different from the ones they have been derived from is under scrutiny, the existing literature shows that the addition of uterine artery Doppler enhances the predictive accuracy of the models [8].

Evidence is emerging that early administration of aspirin reduces the incidence of severe disease in women identified to be at high risk according to the first trimester screening for pre-eclampsia [9-11]. In consequence it is likely that in the near future first trimester uterine dopplers will be incorporated into the routine 11-13 weeks' scan. Recently FIGO advocated first trimester screening and administration of aspirin in high risk pregnancies in order to reduce the maternal mortality due to PET particularly in low income countries [12].

Given the role of the uterine artery (UA) dopplers in the prediction models it becomes important to assess the feasibility and the reproducibility of the measurement. Guidelines have been proposed to standardize the technique of UA Doppler studies at 11-13 weeks and to ensure conformity [13,14]. Few recent studies abiding to the suggested technique have explored UA-PI reproducibility at 11-13 weeks [15-17]. Our aim was to study and compare the transabdominal and the transvaginal approach of measuring first trimester UA Dopplers.

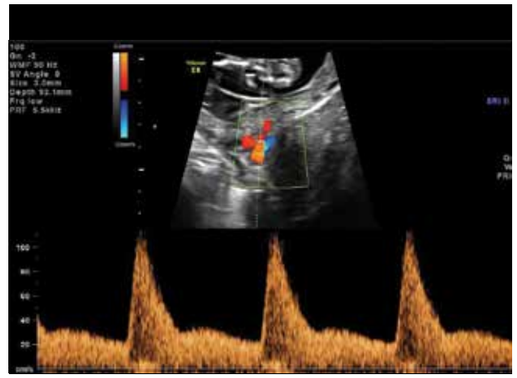

Figure 1a. *Transabdominal view of the uterine artery at 12 weeks of gestation.*

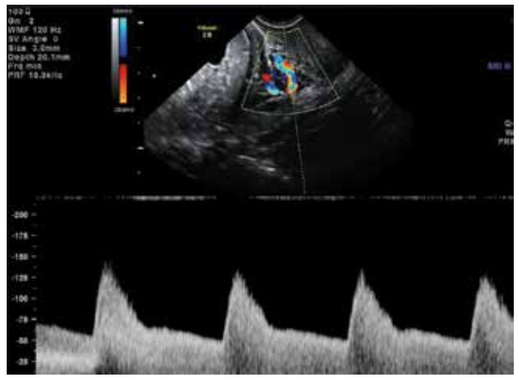

Figure 1b. *Transvaginal view of the uterine artery at 12 weeks of gestation.*

Methods

Prospective observational study conducted between 2018 and 2020. Women presenting for routine first trimester screening at 11-13 weeks of gestation were offered the option of participating in the study and consent was obtained.

As per protocol transabdominal measurement of the UA Doppler indices as well as transvaginal measurement of the cervical length is offered in all pregnant women examined at 11-13 weeks. The ones that decided to participate in the study had transabdominal (TA) as well as transvaginal (TV) measurements of the UA Doppler indices by two experienced operators (AS and AP). The abdominal UA Doppler examination was performed according to the ISUOG guidelines [14]. Briefly the uterine cervix was identified and the transducer was moved gently to the side in order to visualise the uterine artery by Colour Flow (recognised by the aliasing due to the high velocity flow, Figure 1a). Care was taken to maintain an insonation angle less than 30°. At least three consecutive cycles were obtained, the pulsatility index was measured and recorded and the process was repeated for the other side. Similarly for the transvaginal approach the internal cervical os was identified and the probe moved slightly to the side until the uterine vessel was seen using Colour Flow at the level of the internal

Table 1.Intraclass correlation coefficient (ICC) and paired differences among transabdominal (TA) and transvaginal (TV) measurements. A=operator A, B=operator B, RT=right side, LT=left side, 1=first measurement, 2=second measurement

	TA		TV					
A	**Mean**	**SD**	**Mean**	**SD**	**P Paired t-test**	**ICC**	**95% CI**	**P**
RT1	1.61	0.57	1.64	0.55	0.367	0.82	0.77 - 0.86	<0.001
LT1	1.69	0.62	1.74	0.61	0.174	0.80	0.73 - 0.84	<0.001
RT2	1.65	0.61	1.63	0.56	0.655	0.83	0.78 - 0.87	<0.001
LT2	1.71	0.60	1.68	0.54	0.376	0.83	0.77 - 0.87	<0.001
B								
RT1	1.57	0.53	1.60	0.53	0.308	0.80	0.74 - 0.85	<0.001
LT1	1.64	0.59	1.68	0.52	0.158	0.86	0.82 - 0.89	<0.001
RT2	1.55	0.48	1.57	0.53	0.390	0.82	0.77 - 0.86	<0.001
LT2	1.66	0.60	1.66	0.55	0.984	0.86	0.82 - 0.89	<0.001
Both operators								
RT1	1.59	0.55	1.62	0.54	0.173	0.82	0.77 - 0.84	<0.001
LT1	1.67	0.60	1.71	0.57	0.054	0.83	0.79 - 0.86	<0.001
RT2	1.60	0.55	1.60	0.54	0.815	0.83	0.79 - 0.86	<0.001
LT2	1.68	0.60	1.67	0.54	0.524	0.84	0.81 - 0.87	<0.001

Table2. Intra-observercorrelation coefficient (ICC) for transabdominal (TA) and transvaginal (TV) measurements for operator A =A and operator B=B, RT=right side, LT=left side, 1=first measurement, 2=second measurement.

	ICC	95% CI	P
A			
TA: RT1 - RT2	0.91	0.88 - 0.93	<0.001
TA: LT1 - LT2	0.89	0.86 - 0.92	<0.001
TV: RT1 - RT2	0.93	0.91 - 0.95	<0.001
TV: LT1 - LT2	0.90	0.87 - 0.92	<0.001
B			
TA: RT1 - RT2	0.87	0.83 - 0.90	<0.001
TA: LT1 - LT2	0.92	0.89 - 0.94	<0.001
TV: RT1 - RT2	0.96	0.95 - 0.97	<0.001
TV: LT1 - LT2	0.93	0.91 - 0.95	<0.001

Table 3. Inter-observer correlation coefficient (ICC) for transabdominal (TA) and transvaginal (TV) measurements between operator A =A and operator B=B, RT=right side, LT=left side.

	ICC	95% CI	P
RT			
TA: A vs B operator	0.82	0.77 - 0.86	<0.001
TV: A vs B operator	0.91	0.88 - 0.93	<0.001
LT			
TA: A vs B operator	0.87	0.84 - 0.90	<0.001
TV: A vs B operator	0.82	0.77 - 0.86	<0.001

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Table 4. 95% confidence intervals of the limits of agreement (LOA) between operators for uterine pulsatility index measurements of the uterine arteriesat 11 to 13 weeks. 1=first measurement, 1=second measurement, RT=right uterine artery, LT=left uterine artery.

	ICC
RT	
TA: A vs B operator	-0.69-0.68
TV: A vs B operator	-0.47-0.51
LT	
TA: A vs B operator	-0.72-0.69
TV: A vs B operator	-0.59-0.63

Table 5.95% confidence intervals of thelimits of agreement (LOA) between the transvaginal and transabdominal technique of measuring uterine artery pulsatility index. 1=first measurement, 1=second measurement, RT=right uterine artery, LT=left uterine artery.

	LOA
RT 1	-0.89 to 0.84
RT 2	-1.35 to 1.45
LT 1	-0.85 to 0.84
LT 2	-0.83 to 0.85

os (Figure 1b). The uterine vessel was recognised by the features described previously. Women were asked not to void before the abdominal ultrasound scan whereas the transvaginal scan was performed with an empty bladder.

The first operator completed and stored his/hers measurements and subsequently the second operator entered the room and repeated the same process without being aware of the previous results. The UA-PI was measured after the examination in the stored images by manual tracing. A GE Voluson E8 machine was used for the study.

In two cases abdominal measurements could not be obtained because of maternal adiposity and these subjects were excluded from the analysis.

Statistical analysis

Quantitative variables are expressed as mean values (SD). Intra and inter-observer variability of the UA-PI were evaluated with the computation of the intra-class correlation coefficients (ICC) for random effects models and the Bland-Altman 95% confidence intervals (CI) for limits of agreement (LOA) [18-20]. It has been generally accepted that ICC equal or lower to 0.40 indicate poor to fair agreement, 0.41-0.60 moderate agreement, 0.61-0.80 good agreement and over 0.80 excellent agreement [19]. Paired t-tests were used to investigate differences in mean values among the two measurements techniques (TA and TV). Left and right uterine vessels are analysed separately. Agreement between the two measurements techniques was further assessed by Bland-Altman 95% confidence intervals (CI) for limits of agreement (LOA). The 95% CI for LOA indicates that 95% of the differences fall between these two limits.

All p values reported are two-tailed. Statistical significance was set at 0.05 and analyses were conducted using SPSS statistical software (version 22.0).

Results

The study group consisted of 221 singleton pregnancies at 11 to 13 gestational weeks. There were 125 (56.5%) nulliparous women, median weight and height were 64 kgr and 163 cm respectively and median CRL was 62mm. Mean UA-PI was 1.63 for the TA and 1.66 for the TV route. The mean values for TA and TV measurements along with paired comparison between the TA and TV are presented in Table 1. No significant paired differences were found between TA and TV measurements ($p>0.05$) and ICC were over 0.8 in all comparisons ($p<0.001$), indicating good agreement among the two techniques. Intra-observer ICC between the first and second measurements of each operatorranged from 0.89 to 0.91 for operator A and from 0.87 to 0.96 for operator B (Table 2). The ICC for inter-observer agreement ranged from 0.82 to 0.91(Table 3). ICC for intra and inter-observer variability was not influenced by maternal BMI for TA nor TV measurements. LOA between operators are presented in Table 4 and LOA between techniques are presented in Table 5.

Discussion

The study examined a large sample of singleton preg-

nancies at 11-13 weeks recruited from the routine obstetric population presenting for the 11-13 weeks' scan. The measurements were performed by experienced operators who followed the ISUOG and FMF guidelines and were blind to each other's results. We chose to assess each PI separately rather than use the mean of the right and left measurements which could overestimate the reproducibility of the method. We found that UA-PI measurements have good reproducibility (ICC between 0.87 and 0.96 for intra and between 0.82 and 0.91 for inter-observer agreement). The transvaginal route seems to perform better although the difference was not significant. It is important to note that TA measurement was not possible in two obese subjects not included in the study. We have observed no significant difference in paired measurements acquired by TA or TV scan.

Until recently these results would be considered to indicate good to excellent agreement as they mean that more than 80% of the difference between Ut-PI measured by different operators is a 'true difference' whereas the remaining 20% can be attributed to physiological variation or error of the method. In the last decade the TRUST study suggested, somehow arbitrarily, stricter criteria for defining good reproducibility in obstetric Doppler measurements which would be difficult to be met by any fetal/maternal Doppler measurement and could discredit their use in clinical practice [21,22]. The new criteria on interpreting ICC (requiring ICC>95% for clinical use) have been criticized mainly for the failure to take into account the physiological variation of blood flow patterns [23, 24]. The authors acknowledge that LOA may be a better tool for assessing repeatability in Doppler measurements [23]. Indeed In our study LOA showed good agreement between operators with a range of -0.7 to 0.7.

Our results are consistent with the ones reported by-Marchi et al on 101 singleton pregnancies [17]. They observed very similar ICC for the TA and TV approach regarding intra-observer agreement whereas the inter-observer ICC of our study was comparable to the one achieved by the more experienced operators. Almost identical results are also reported by Ferreira et al on 97 first trimester pregnancies [16]. It is of interest that the two largest, recent studies as well as ours give very close estimates as to the reproducibility of the Ut-PI measurements with ICC between operators at about 0.8 at least and LOA between -0.8 and 0.8. The results are virtually identical for the experienced operators and indeed the Marchi study demonstrated that the only factor affecting reproducibility was the experience of the operator.

We did not find a significant difference in the mean Ut-PI between the TAS and the TVS approach. The issue was approached by three previous studies and the results are controversial [16,17,25]. The possible explanation for higher TAS Ut-PI found by two previous studies is that the TVS approach measures closer to the systemic circulation. Obviously it would not be possible to interrogate the uterine by TAS and TVS at exactly the same spot, but in our view both approaches target the uterine vessels at about the same level, provided that strict criteria are observed.

A possible disadvantage of our study is the extensive experience of the operators which may make the results not applicable to different settings. It is therefore reassuring that similar results were obtained by well-trained sonographers in a non-academic setting [17].

The uterine artery Doppler studies have at least moderate to good reproducibility, although the criteria to judge this are a matter of debate. Perhaps the real clinical issue however is how reproducible is the risk result that the patient is provided with and this is an interesting question for research. ■

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