Published in final edited form as:

Ultrasound Obstet Gynecol. 2021 November ; 58(5): 722–731. doi:10.1002/uog.23112.

Cross-modality and in-vivo validation of 4D flow MRI evaluation of uterine artery blood flow in human pregnancy

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Abstract

Objectives—Clinical assessment of uterine artery (UtA) hemodynamics is currently limited to ultrasound (US) Doppler velocimetry. We previously demonstrated the feasibility of 4D flow magnetic resonance imaging (MRI), which allows flow quantification throughout the entire vessel, to evaluate UtA hemodynamics during pregnancy. In this study, we seek to further validate the physiologic relevance of 4D flow MRI measures of UtA blood flow rate by exploring their associations with pregnancy outcomes relative to US-based metrics.

Methods—This was a cross-sectional study of 87 singleton pregnant women, enrolled between May 2016 and April 2019, who underwent a 4D flow MRI scan to measure UtA pulsatility index (PI) and blood flow rate (in mL/min). UtA PI was also measured using US. The primary outcome was a composite (COMP) of either preeclampsia (PEC), small for gestational age (SGA), or both PEC+SGA. The secondary outcomes were PEC and SGA individually. Wilcoxon rank-sum tests were performed to study the ability of MRI-flow, MRI-PI, and US-PI to distinguish between no disease versus disease. Linear regression was also performed to study MRI-flow versus gestational age (GA).

Results—Of the 74 subjects that were analyzed, 18 subjects were COMP: PEC (n=3), SGA (n=11), and both PEC+SGA (n=4). Additionally, one subject excluded from the analysis had

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an intrauterine fetal demise (IUFD). When comparing subjects with and without COMP, no differences in maternal age, body mass index (BMI), nulliparity, gravidity, or race were found. In 66 of the 74 subjects US data was also available. Both median MRI-PI (0.95 vs. 0.70, $p<0.01$) and median US-PI (0.95 vs. 0.73, $p<0.01$) were significantly increased in subjects with COMP compared to no COMP. UtA blood flow rate, as measured by MRI, did not significantly increase from 2nd to 3rd trimester (median flow [interquartile range]=543[419,698] vs. 575[440,746] mL/min, $p=0.77$), but it was significantly lower in COMP compared to no COMP (median flow [interquartile range]=486[366,598] vs. 623[457,749] mL/min, $p=0.04$). The AUCs for MRI-flow, MRI-PI, and US-PI in predicting COMP were comparable (0.69, 0.74, and 0.73) with non-significant differences among the three AUCs ($p=0.87$).

Conclusions—4D flow MRI can yield physiologic measures of UtA blood flow rate and PI that are associated with adverse pregnancy outcomes. This may open new avenues in the future to explore more robust MRI-based evaluation of UtA hemodynamics in pregnancy.

Keywords

Uterine artery; Doppler ultrasound; 4D flow MRI; preeclampsia; intrauterine growth restriction

Introduction

Doppler ultrasound (US) assessment of the maternal uterine arteries (UtAs) has shown promising results for predicting risk of adverse pregnancy outcomes^{1,2}, but the multiparametric models required for these assessments are more complex than current clinical US practice. US also has inherent limitations, such as its sensitivity to the angle between the device and the interrogated flow direction, that preclude accurate and reproducible assessment of UtA remodeling and hemodynamic function during pregnancy³. The Nulliparous Pregnancy Outcomes Study: Monitoring Mother-to-be (nuMoM2b) study found UtA Doppler US to have low positive predictive value in predicting small-for-gestational-age neonates⁴. Other studies have reported variable results depending on gestational age of onset of preeclampsia⁵ and superimposed fetal growth restriction⁶. Mounting evidence suggests that some women with abnormal trophoblast invasion have normal UtA Doppler waveforms while others with abnormal UtA Doppler waveforms have healthy deliveries^{7,8}. Thus, a more robust tool to investigate UtA remodeling and hemodynamics during pregnancy is still needed.

Four-dimensional (4D) flow magnetic resonance imaging (MRI) time-resolves each component of the blood flow velocity vector along with morphological data in a single, non-invasive, non-ionizing scan⁹. This is advantageous given the complex hemodynamic nature in various cardiovascular conditions. Therefore, it has successfully been used to measure advanced parameters such as pressure and wall shear stress¹⁰⁻¹³. During pregnancy, a key advantage of 4D flow MRI is its large spatial coverage allowing for evaluation of the entire course of the UtA. We previously demonstrated that this modality is technically feasible in pregnant women¹⁴ but did not correlate UtA flow measurements with pregnancy outcomes. In this study, we sought to further validate the 4D flow MRI measures of UtA blood flow by exploring the association of these measures with adverse pregnancy outcomes and by comparing these associations with similar associations drawn from Doppler US.

Methods

Study participants

A total of 87 singleton pregnant subjects were enrolled between May 26, 2016 and April 25, 2019 in this cross-sectional study approved by the institutional HIPAA-compliant Institutional Review Board. Inclusion criteria included singleton gestations at 15 weeks or greater. Exclusion criteria were: (1) morbid obesity (pre-gravid BMI ≥ 35), (2) major structural fetal anomaly, (3) routine MRI contraindications such as metallic implants/devices and claustrophobia. For some analyses involving comparison with outcomes subjects lost to follow-up after MRI were not included, and subjects with intrauterine fetal demise (IUFD) were analyzed separately from deliveries after 24 weeks with neonates that reached viability. Only subjects whose pregnancies reached viability and whose obstetric outcomes were available were included in analyses comparing MRI to pregnancy outcomes. For analyses involving associations between US-pulsatility index (PI) and pregnancy outcomes, subjects without US scan were not included. Pregnancy outcomes were extracted from the medical record. The primary outcome was a composite (COMP) of either or both preeclampsia (PEC), as defined by the American College of Obstetricians and Gynecologists criteria¹⁵, and small for gestational age (SGA) defined as birth weight $<10^{\text{th}}$ percentile¹⁶. Secondary outcomes were PEC and SGA individually. Both MRI-PI and MRI-flow were each analyzed as predictors of the outcomes, while US-PI was also analyzed as a predictor of outcome for comparison.

Measurement of PI and flow with 4D flow MRI

Prospective ECG-gated 4D flow MRI¹⁴ at 1.5T (Avanto, Siemens Healthineers, Erlangen, Germany) was acquired of the UtAs and external iliac arteries near the internal orifice of the cervix (Fig. 1) using a 12-channel spine and two 4-channel body matrix coils. The sequence parameters were: flip angle=8°, repetition time/echo time=5.5/3ms, voxel size=1.25x1.25x1.25mm³, field-of-view=320x200x60mm³, bandwidth per pixel=445-455 Hz/pixel, segments/shot=2, temporal resolution=42.4-46.4ms, acceleration factor=4.7, velocity encoding (VENC)=100 cm/s, number of cardiac phases=10-18, and scan time=12-20 minutes depending on subject's heart rate. Noise was removed from the velocity maps with thresholding and four planes distributed along each vessel were manually prescribed to extract velocity maps at each plane location (Ensign, CEI; Apex, NC). On each velocity map, the UtA was manually contoured using custom software (Matlab; The MathWorks, Natick, MA, USA). MRI-PI was computed from the spatial maximum MRI velocity waveforms as $PI = (v_{max} - v_{min}) / \bar{v}$ and averaged across the four planes for each vessel, where v_{max} =temporal maximum velocity, v_{min} =temporal minimum velocity, and $\bar{v}$ =temporal mean velocity. UtA flow rate (mL/min) was computed from the spatial mean MRI velocity waveforms and vessel cross-sectional area and averaged across the four planes for each vessel (Fig. 1). More details about the MRI acquisition, post-processing procedure, repeatability of 4D flow MRI scans, and interobserver reproducibility of post-acquisition measures were previously described¹⁴.

Measurement of PI with Doppler US

Each subject was positioned in semi-recumbent supine. The UtAs were scanned using the C4-8 transabdominal probe of a GE Voluson E10 (GE Healthcare, Wisconsin, United States) US machine by a Maternal Fetal Medicine clinician (N.S.) with extensive experience in prenatal US. An average of three measurements of UtA Doppler PI values were recorded bilaterally.

Statistical Analysis

MRI-flow, MRI-PI, and US-PI values are reported as median and interquartile range (IQR, 25%-75%) or mean and standard deviation (SD). Scatter plots of MRI-flow versus gestational age (GA) were generated and R-squared calculated from fitting linear regression models. Wilcoxon rank-sum test was used to investigate differences in MRI-flow, MRI-PI, and US-PI between the pregnancies with and without one of the three outcomes (COMP, PEC, and SGA). We also report adjusted results after accounting for demographic parameters that were statistically significantly different between COMP and no COMP. In addition, Spearman's correlation and Wilcoxon signed-rank test were used to compare between MRI-PI and US-PI. Receiver-operating characteristics (ROC) curves and the corresponding area under the curve (AUC) were generated for MRI-flow, MRI-PI, and US-PI across outcomes, and a Wald test was used to compare the AUC values associated with MRI-PI and US-PI. Statistical significance was considered at $p < 0.05$. Statistical analysis was performed using Stata 14.2 (College Station, TX).

Results

Delivery Outcomes and Exclusions

After recruitment for MRI, 4D flow post-processing, and applying exclusions for analysis, data from 74 pregnant subjects were analyzed for both UtAs (Fig. 2, Table 1). The remaining subjects included one with IUFD and 7 subjects lost to follow-up. Of the 74 subjects, 18 developed a COMP outcome, including 3 with PEC, 11 with SGA, and 4 with both. In 66 of the 74 subjects US Doppler data was acquired on the same day as MRI (Fig. 2, Table 2). No significant demographic differences between COMP and no COMP were found in terms of age, race, BMI, nulliparity, and gravidity (Table 2). However, in comparison to no COMP subjects, the COMP subjects were scanned at later GA and delivered at earlier GA with lower birthweight. They also had higher rates of chronic hypertension (CHTN). 39 out of the 74 subjects (35 out of the 66 subjects) were also reported in a previous study¹⁴.

MRI-flow with GA and Delivery Outcomes

Median total UtA blood flow (sum of left and right UtA flow) was 592 (IQR 441-742) mL/min in the 74 subjects. There was no correlation with GA ($y = -0.47x + 614.67$, $R^2 < 0.01$, $p = 0.91$). Fig. 3 shows a scatterplot of MRI-flow values along GA. The subject with IUFD imaged at 15 weeks gestation had lower flow than the other subjects at 109.5 mL/min with normal US-PI of 1.98 and MRI-PI of 1.92. When evaluating COMP and no COMP subjects separately, median UtA blood flow was 486.1 (IQR 598.2-366.1) mL/min in the 18 COMP subjects and 623.8 (IQR 456.6-748.6) mL/min in the 56 no COMP subjects. As a

group, the COMP subjects had slightly lower flow than the no COMP group, particularly in the second trimester. No correlations between UtA flow and GA were found in the COMP group ($y=6.14x+314.75$, $R^2=0.06$, $p=0.34$) and no COMP group ($y=1.20x+599.67$, $R^2<0.01$, $p=0.82$). The two-sample Wilcoxon rank-sum test showed a reduction in MRI-flow in COMP subjects ($p=0.04$), with a trend towards reduction when examining PEC ($p=0.08$) and SGA ($p=0.08$) individually. Box-and-whisker plots of MRI-flow in the 74 subjects with delivery outcomes are available in Fig. 4. After adjusting for GA (at MRI) and CHTN, mean $\pm$ SD MRI-flow was 496.9 ± 54.6 mL/min in COMP and 635.0 ± 29.8 mL/min in no COMP subjects ($p=0.03$). In the 18 COMP subjects, there was an average of 40 ± 35 days between the imaging exam and delivery. In 16 of the 18 subjects, diagnoses of PEC and SGA were recorded at delivery.

MRI-PI and US-PI with Delivery Outcomes

A comparison between MRI-PI and US-PI showed a moderate Spearman's correlation with $\rho=0.69$ ($p<0.01$) and significant bias with median MRI-PI=0.75 (IQR 0.63-0.94) and median US-PI=0.78 (IQR 0.67-1.03) ($p<0.01$). Both MRI and US techniques were able to detect increased PI in the 15 subjects with COMP (out of 66 subjects) (MRI-PI: $p<0.01$; US-PI: $p<0.01$) (Fig. 4). These differences in both MRI and US PI remained significant when looking at PEC (MRI-PI: $p<0.01$; US-PI: $p=0.02$) and SGA (MRI-PI: $p=0.03$; US-PI: $p<0.01$) as individual outcomes as well. After adjusting for GA (at MRI and US) and CHTN, MRI-PI was 1.02 ± 0.07 for COMP and 0.72 ± 0.04 for no COMP ($p<0.01$); US-PI was 1.23 ± 0.1 for COMP and 0.81 ± 0.05 for no COMP ($p<0.01$).

MRI-flow, MRI-PI, and US-PI ROC Curves

The ROC AUCs provided by MRI-flow for no COMP, no PEC, and no SGA were 0.66, 0.69, and 0.64, respectively for the 74 subjects (Fig. 5). The AUC values from MRI-PI vs. US-PI for the following groups in the 66 subjects were also compared. Further, no significant difference was found between the two modalities: COMP (0.74 vs. 0.73, $p=0.94$), PEC (0.84 vs. 0.75, $p=0.31$), and SGA (0.69 vs. 0.75, $p=0.40$) (Fig. 6). In Fig. 7, the ROC curves from MRI-flow, MRI-PI, and US-PI were compared in the 66 subjects which show no significant difference in predicting COMP ($p=0.87$).

Discussion

The principal finding of this study is concordance between 4D flow MRI and US in distinguishing between pregnancies with no COMP and COMP. We successfully applied 4D flow MRI to the UtAs and found increased MRI-PI in pregnancies that went on to develop SGA and PEC¹⁷⁻²⁰, outcomes associated with impaired trophoblastic invasion. US-PI is used to measure UtA resistance as a reflection of downstream trophoblast invasion^{3, 17, 21, 22}. As compared to US, 4D flow MRI provides the spatial coverage to visualize the length of the UtAs, measure lumen area, and decompose blood velocity in three orthogonal directions. In this study, both US and MRI-PI showed similar prediction of adverse outcomes based on ROC analysis. While US is more accessible, our data suggests that MRI-PI values are physiologically relevant, providing support for its continued development as a tool for assessing placental health.

We observed that MRI-flow was lower in COMP than no COMP subjects. The no COMP vs. PEC/SGA group comparisons showed the same trend but sample size may not have been large enough to demonstrate significance. Elevated UtA PI may be a concern during late pregnancy because high resistance limits delivery of oxygenated blood to the placenta^{3, 21, 22}. UtA flow is a more direct measurement of perfusion than PI. We previously demonstrated the feasibility of measuring UtA flow during pregnancy with 4D flow MRI¹⁴. The one IUFD subject in our study was found to have low UtA flow despite normal MRI/US-PI compared to the cohort of live births. Our findings are consistent with the notion that reduced total UtA flow rate to the placenta is linked to poor pregnancy outcomes. While studies of US-based measurements of UtA flow have reported lower flow in PEC²³⁻²⁶ and SGA^{27, 28}, technical challenges have precluded clinical use of US-based flow. US is more user-dependent than MRI and sensitive to body habitus, angle of insonation, and instrument gain artifacts. As lumen diameter is a significant contributor to accurate flow measurements, flow measurements may be difficult to reproduce since lumen walls may not be clearly resolved²³. Furthermore, since the UtAs are often tortuous, absolute measures such as flow rate that depend on measurement angle are challenging to interrogate²³.

We did not observe a significant change in MRI-flow with GA, which we previously attributed to our subject population being imaged only in the second/third trimester¹⁴, since prior work suggested that most of the increase in UtA flow occurs in the first trimester^{25, 29, 30}. However, several studies have also reported an increase in UtA flow measured by US in the second and third trimester³¹⁻³⁴. Our findings suggest that low MRI-flow measures are meaningful and associated with adverse pregnancy outcomes, though intersubject heterogeneity in our population may have weakened the MRI-flow vs. GA relationship in our cross-sectional study. Although the mean GA at MRI was significantly later for the COMP than no COMP group ($p < 0.01$, Table 2), this did not mask the effect of significantly lower MRI-flow in COMP than no COMP ($p = 0.04$). Since GA is a plausible confounder^{28, 33}, we adjusted the analysis for GA and significant group differences persisted ($p = 0.03$).

In this study, US-PI showed an absolute positive bias over MRI-PI ($p < 0.01$), consistent with our previous report¹⁴, which can be attributed to MRI/US differences in spatiotemporal resolution, subject body positioning, and location of measurement along the UtA. Even though MRI-PI and MRI-flow AUC performances were comparable to US-PI (Fig. 7), UtA Doppler is still largely an investigational tool. US-PI has been found to have inconsistent performance especially in first trimester pregnancy and unselected, low risk populations^{4, 35}. In Fig. 8, we show an example of the 4D flow geometry and pathlines in healthy and PEC subjects. This approach has the advantage of deeper penetration and larger field-of-view, thus able to more comprehensively visualize the uterine vessels for localization.

4D flow MRI has been gaining clinical attention, showing utility in assessing various cardiovascular diseases⁹. For example, 4D flow MRI has been shown to measure wall shear stress (WSS), which can be utilized as a meaningful tool for assessing and managing intracranial aneurysms^{36, 37}. For our purposes, the pathophysiology of PEC also involves inherent vessel wall dysfunction^{18, 19, 38-41}. Further development of 4D flow MRI for assessing the UtAs in pregnancy can lead to clinically impactful tools to aid in risk

stratification, identifying early signs of pathology, and guiding future clinical trials aimed at exploring potential preventive and treatment strategies.

Our study had a high percentage of COMP subjects (18/74, 24%) compared to the 10-15% prevalence of PEC and SGA in the general population, but this is expected because the University of Pennsylvania serves a community with a large population of black women, and black race is a risk factor for PEC/SGA⁴². One limitation of this study is that it is cross-sectional, making it difficult to distinguish between intersubject variability and gestational MRI-flow progression. Longitudinal studies can better characterize changes in UtA MRI-PI/flow. Another limitation is that the 4D flow MRI sequence used in this study had limited spatial ($1.25 \times 1.25 \times 1.25 \text{ mm}^3$; ~3-4 voxels across the UtA diameter) and temporal resolution (42 ms), potentially limiting the accuracy of PI and flow rate measurements. We measured a median UtA flow of 623 mL/min in the no COMP subjects, which seemed lower than the values reported by US^{28, 33} and 2D phase contrast MRI⁴³. While it appeared possible that US overestimated mean velocity over the cross-sectional area by sampling the center of the vessel, we may have underestimated flow by using lower spatial and temporal resolution with a 1.5T rather than the 3T magnetic field strength used for 2D phase contrast MRI⁴³. We believe this was a systematic bias that affected measurements in both COMP and no COMP subjects and we did demonstrate repeatability in a previous study¹⁴. Fortunately, substantial progress in 4D flow MRI is being made to decrease scan time and improve temporal and spatial resolution^{44, 45}. We believe with optimization and technical improvements 4D flow MRI can potentially be useful earlier in gestation.

Conclusions

Effective methods to predict risk of adverse pregnancy outcome are critical to obstetric care. This study demonstrates that 4D flow MRI is comparable to Doppler US in measuring PI and additionally measures flow. Both PI and flow are able to distinguish between pregnancies with PEC, SGA, or both and a reference group. 4D flow MRI is a technique that can serve as the foundation for more robust tools to better understand the hemodynamics of the UtAs during pregnancy.

Acknowledgements

We gratefully acknowledge support from U01-HD087180, DGE-1321851, T32-EB009384, P41-EB015893, R00-HL108157, R01-HL137984, and R00-HD074649. We also thank the MRI technologists, Maternal Fetal Medicine research coordinators, and pregnant volunteers who participated this study at the Hospital of the University of Pennsylvania.

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Contribution

What are the novel findings of this work?

This study is the first to provide evidence that uterine artery MRI pulsatility index and MRI flow measurements can distinguish between normal and adverse pregnancy outcomes.

What are the clinical implications of this work?

The preliminary findings support the potential of 4D flow MRI as an effective clinical tool for risk stratification in early pregnancy.

Figure 1.

Diagram outlining methodological workflow: a) MRI localizer, b) time-of-flight MRI angiogram, and c) 4D flow MRI were collected from UtAs. 4D flow post-processing consisted of extracting velocity waveforms from each plane (example for Plane R1 shown in (d)). e) Transabdominal Doppler US was collected from the UtAs. MRI-flow was computed by multiplying cross-sectional area (CSA) by mean velocity ($\bar{v}$) from 4D flow data. MRI-PI and US-PI were computed from 4D flow MRI and US waveforms, where $v_{\max}$ =systolic maximum velocity and $v_{\min}$ =diastolic minimum velocity. For each subject, MRI-flow was averaged across four planes in each UtA and added together for total bilateral MRI-flow used in subsequent statistical analysis. MRI-PI and US-PI were also averaged from repeated measurements or planes and additionally averaged from both UtAs.

Figure 2.
Diagram of exclusion criteria for analysis

Figure 3.

Scatterplot of MRI-flow vs. GA in 74 pregnant subjects with significantly lower median total uterine artery flow in no COMP compared to COMP subjects (dashed lines).

Correlation was not found between MRI-flow and GA for all subjects, COMP, and no COMP. The red "X" indicates the total uterine artery flow of the IUFD subject for visual comparison.

Figure 4.

In the 74 subjects with delivery outcomes recorded, we present the box-and-whisker plots of MRI-flow showing difference in a) no COMP vs. COMP ($p=0.04$), b) no COMP vs. PEC ($p=0.08$), c) no COMP vs. SGA ($p=0.08$). In the 66 subjects with US data available, we present box-and-whisker plots showing difference in d,g) no COMP vs. COMP by MRI-PI ($p<0.01$) and US-PI ($p<0.01$), e,h) no COMP vs. PEC by MRI-PI ($p<0.01$) and US-PI ($p=0.02$), and f,i) no COMP vs. SGA by MRI-PI ($p=0.03$) and US-PI ($p<0.01$). Red “X” shows MRI-flow, MRI-PI, and US-PI for the IUFD subject.

Figure 5. MRI-flow ROC curves for: a) no COMP with AUC=0.66, b) no PEC with AUC=0.69, and c) no SGA with AUC=0.64

Figure 6. ROC curves from MRI-PI for a) COMP with AUC=0.74, c) PEC with AUC=0.84, and e) SGA with AUC=0.69. ROC curves from US-PI for b) COMP with AUC=0.73, d) PEC with AUC=0.75, and f) SGA with AUC=0.75.

Figure 7.

Comparison of the ROC curves from MRI-flow, MRI-PI, and US-PI in 66 subjects for COMP. They show no statistically significant difference ($p=0.87$).

Ultrasound Obstet Gynecol. Author manuscript; available in PMC 2021 November 03.

Table 1:

Demographic information for subjects with delivery info, divided into subsets COMP and no COMP. BMI=body mass index, CHTN=chronic hypertension, GDM=gestational diabetes mellitus, GA=gestational age, GHTN=gestational hypertension, PEC=preeclampsia, SGA=small-for-gestational age, PI=pulsatility index, %=percentage, std=standard deviation, IQR=interquartile range (25%-75%), p-values reported from two-sample Wilcoxon rank-sum test,

	Cohort with Delivery Info	COMP	No COMP	p-value
N (%)	74 (100)	18 (24)	56 (76)	
Age (std)	27.5 (6.2)	26.2 (5.9)	27.9 (6.3)	0.315
Race				0.223
Black (%)	53 (72)	16 (89)	37 (66)	
White (%)	16 (22)	2 (11)	14 (25)	
Other (%)	5 (7)	0 (0)	5 (9)	
BMI (IQR)	30.2 (26.2-33.3)	30.2 (25.2-34.6)	30.2 (26.2-32.7)	0.99
Nulliparity (%)	41 (55)	9 (50)	32 (57)	0.596
Gravidity (IQR)	2 (1-3)	2 (1-3)	2 (1-3)	0.521
CHTN (%)	6 (8)	4 (22)	2 (4)	0.028*
GDM (%)	6 (8)	2 (11)	4 (7)	0.592
GA at delivery (IQR)	39.3 (37.9-40.1)	37.3 (37.1-39.0)	39.5 (38.4-40.6)	0.001*
Birthweight (g) (IQR)	3147.5 (2680-3620)	2375 (2015-2685)	3310 (3072.5-3679.5)	0.001*
GHTN (%)	16 (22)	6 (33)	10 (18)	0.165
PEC (%)	7 (9)	7 (39)	0 (0)	0.001*
SGA (%)	15 (20)	15 (83)	0 (0)	0.001*
GA at MRI (IQR)	28.4 (23.6-32.9)	31.6 (25.7-36.4)	26.6 (23.1-31.2)	0.009*
Total Uterine Artery Flow (mL/min) - MRI (IQR)	591.8 (440.9-742.5)	486.1 (366.1-598.2)	623.8 (456.6-748.6)	0.038*

*
p<0.05

Table 2:

Demographic information for subjects with delivery and US info, divided into subsets COMP and no COMP. BMI=body mass index, CHTN=chronic hypertension, GDM=gestational diabetes mellitus, GA=gestational age, GHTN=gestational hypertension, PEC=preeclampsia, SGA=small-for-gestational age, PI=pulsatility index, %=percentage, std=standard deviation, IQR=interquartile range (25%-75%), p-values reported from two-sample Wilcoxon rank-sum test,

	Cohort with Delivery & US Info	COMP	No COMP	p- value
N (%)	66 (100)	15 (23)	51 (77)	
Age (std)	28.1 (6.3)	27.2 (6.0)	28.3 (6.4)	0.542
Race				0.289
Black (%)	46 (70)	13 (87)	33 (65)	
White (%)	15 (23)	2 (13)	13 (25)	
Other (%)	5 (8)	0 (0)	5 (10)	
BMI (IQR)	30.6 (26.2-33.4)	31.3 (25.5-35.0)	30.4 (26.2-32.6)	0.493
Nulliparity (%)	34 (52)	6 (40)	28 (55)	0.31
Gravidity (IQR)	2 (1-3)	2 (1-3)	2 (1-3)	0.675
CHTN (%)	6 (9)	4 (27)	2 (4)	0.021 *
GDM (%)	6 (9)	2 (13)	4 (8)	0.516
GA at delivery (IQR)	39.1 (37.7-40.0)	37.1 (36.7-39.0)	39.4 (38.3-40.3)	0.001 *
Birthweight (g) (IQR)	3142.5 (2685-3640)	2380 (1885-2690)	3350 (3050-3740)	0.001 *
GHTN (%)	16 (24)	6 (40)	10 (20)	0.105
PEC (%)	7 (11)	7 (47)	0 (0)	0.001 *
SGA (%)	12 (18)	12 (80)	0 (0)	0.001 *
GA at MRI and US (IQR)	27.4 (23.4-32.9)	31.6 (25.7-36.4)	25.6 (22.6-31.1)	0.013 *
Uterine Artery PI, Right - US (IQR)	0.71 (0.62-0.99)	0.84 (0.71-1.14)	0.69 (0.58-0.96)	0.015 *
Uterine Artery PI, Left - US (IQR)	0.79 (0.67-0.92)	0.91 (0.76-1.67)	0.78 (0.65-0.87)	0.008 *
Uterine Artery PI, mean - US (IQR)	0.78 (0.67-1.03)	0.95 (0.76-1.37)	0.73 (0.64-0.92)	0.007 *
Uterine Artery PI, Right - MRI (IQR)	0.71 (0.58-0.91)	0.91 (0.67-1.08)	0.68 (0.56-0.87)	0.043 *
Uterine Artery PI, Left - MRI (IQR)	0.75 (0.60-0.94)	0.91 (0.70-1.43)	0.73 (0.56-0.84)	0.014 *
Uterine Artery PI, mean - MRI (IQR)	0.75 (0.63-0.94)	0.95 (0.75-1.13)	0.70 (0.61-0.86)	0.006 *
Total Uterine Artery Flow (mL/min) - MRI (IQR)	616.4 (451.8-748.1)	469.8 (356.4-630.4)	648.2 (480.6-755.4)	0.023 *

*
p<0.05