


Difference between near-field and far-field of middle cerebral artery doppler pulsatility index and peak systolic velocity: a prospective study

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Objective: We purposed to investigate the difference between near-field and far-field of PI (pulsatility index) and peak systolic velocity (PSV) of the middle cerebral artery (MCA) that are important in the management of fetal growth restriction and fetal anemia. **Methods:** This prospective study was conducted with 130 single uncomplicated pregnancies. Doppler was applied to near-and far-field of proximal MCA while PSV and PI were recorded and compared between two sides as well as according to body mass index (BMI) and gestational weeks of participants. **Results:** There was no statistically significant difference between near and far-fields of MCA PI ($P = 0.75$). However, a statistically significant difference in PSV was observed ($P = 0.03$), and this was especially noticeable in women with normal BMI ($P = 0.009$). On the other hand, there was no difference between MCA PI or PSV in women with a BMI higher than 25. Also, no significant difference was observed between groups, which were subcategorized according to gestational weeks. **Conclusions:** Our data suggest that the far-field PSV values may be higher than near-field MCA PSV values; sonographers should bear in mind that while far and near-field PSV can differ, conversely MCA PI can safely be assessed from both the near and far-fields of MCA in case of technical difficulty.

Keywords

Doppler ultrasound; Middle cerebral artery; Peak systolic velocity; Pulsatility index

1. Introduction

Recently, Doppler studies of the middle cerebral artery (MCA) have become crucially important in evaluating fetal well-being and the management of pregnancies [1, 2]. The peak systolic velocity (PSV) of the MCA is the most accepted non-invasive method and was previously proven to be effective in the detection of fetal anemia [3–5]. Furthermore, clinicians extensively apply MCA-PSV-based management in either fetal intrauterine transfusion or timing for delivery [6]. Also, the pulsatility index (PI), an additional Doppler parameter of the MCA, is widely used to assess intrauterine growth-restricted fetuses. The cerebroplacental ratio (CPR) is calculated from the ratio of PI of the MCA to PI of the umbilical artery (UA). It has been identified as a functional marker of both fetal hypoxemia and cerebral redistribution

that is defined as the brain-sparing effect [7, 8]. Abnormal CPR has also been associated with abnormal fetal growth velocity, increased risk for neonatal intensive care unit admission and urgent cesarean delivery for fetal distress after 37 weeks, independent from the fetal weight [9]. CPR and the brain-sparing effect have a considerable impact on managing term fetuses with growth restriction. Therefore, obtaining Doppler flow data of the MCA is vital for the fate of pregnancy. Thus, accurate measurement is an essential part of the service that clinicians should offer to patients [10].

Measuring MCA Doppler values is usually more complicated than UA Doppler studies [11]. Perhaps the most important difference between the two Doppler studies is the insonation angle. According to the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG), the insonation angle is defined as the angle of the ultrasound beam relative to the direction of blood flow. This angle is important and must be carefully adjusted, especially in the case of PSV measurement of the MCA. The proximal portion of the MCA, which is 2 mm away from the internal carotid artery, is the preferred measurement location [12]. Additionally, when studying the MCA PSV with Doppler values, the insonation angle should be as close to 0° as possible. However, according to the literature, the MCA PI is thought to be independent of this angle but dependent on the portions of the vessel [2, 13].

Appropriate techniques for obtaining fetal MCA Doppler waveforms have been previously described in the literature [11, 12]. There are several studies on this subject regarding measurements from different locations, such as from the proximal, intermediate, and distal parts of the MCA. However, to our knowledge, little information regarding the near and far fields of the MCA has been presented [14, 15]. The purpose of this study is to investigate whether the near-field versus the far-field of the artery matters for Doppler assessment of the MCA PI or PSV.

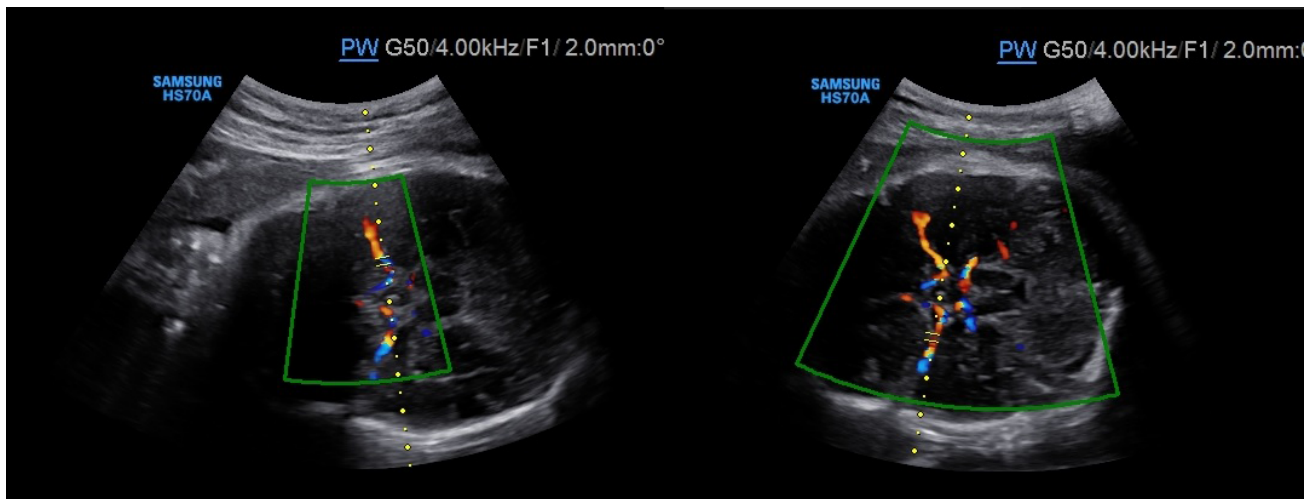


Fig. 1. Doppler measurement technique of MCA from near-and far-fields.

2. Materials and methods

This study was carried out from April to November 2019 in the department of perinatology at Tepecik Training and Research Hospital in Izmir, Turkey. The establishment's ethics committee approved the study with the registration number 2019/14-21. All participants gave written informed consent.

2.1 Patient selection

Patients with a gestational range of 21-39 weeks were included in the study. The gestational age was calculated from the last menstrual period and confirmed by first-trimester sonography. Multiple gestations and fetuses with major abnormalities, aneuploidy markers, and women with maternal alloimmunization were excluded. Pregnancies complicated by oligohydramnios, polyhydramnios, all types of diabetes, hypertension, abnormal fetal growth (restricted or large for their gestational age), and UA Doppler abnormalities were excluded. UA systole/diastole ratio (S/D) and PI Doppler assessment were calculated for all patients, and patients with UA Doppler S/D and PI values greater than the 95th percentile were excluded. All examinations were made by a single operator to exclude inter-observer and intra-observer differences.

2.2 Technical approach

The ultrasound machine used for this study was the Samsung Ultrasound System HS70A (Samsung Medison Company, Republic of Korea) with a CA1-7A curved array abdominal transducer. Recordings were performed during the absence of fetal movement or respiratory movement. No pressure was applied to the fetal head. At first, the UA Doppler assessment was conducted. In the absence of fetal breathing and body movements, a free loop from the placental end of the umbilical cord as close to 0° as possible was used for UA Doppler. Afterwards, the MCA Doppler assessment was made according to the standard technique as defined in the ISUOG Practice Guidelines [11]. A clear axial

section of the fetal brain was presented. Thalamus and sphenoid bone wings were obtained and magnified to at least 50% of the screen. Colour Doppler was executed, and all the components of the Willis polygon, including the MCA, were observed. A pulse wave Doppler gate with a sample volume gate of 1 mm was placed at a proximal section of the MCA, 2 mm away from its origin from the internal carotid artery. The angle of insonation was kept as close as possible to 0°, but the maximal angle of insonation did not exceed 30°; angle correction was applied if necessary (Fig. 1) [12]. The MCA Doppler assessment was conducted to the proximal third of the near field and the proximal third of the far-field, respectively. At least ten serial waveforms from the best-acquired image were recorded, and the Doppler parameters were calculated using the software provided with the equipment. Each participant had only one measurement during their pregnancy period. The Doppler assessment was executed on the MCA, and the PSV, S/D, PI, and resistance index (RI) measurements were calculated automatically by the ultrasound machine software. Also, MoM (multiples of the median) were calculated for all PSV values for both near and far-field of MCA.

2.3 Statistical analysis

Statistical analysis was performed with SPSS version 22 software (IBM Corporation, Armonk, NY). Shapiro-Wilk's test, a histogram and Q-Q plot were examined to assess the data normality. After defining the normality, mean and standard deviation or median, the interquartile range was given for continuous variables. The paired sample *t*-test and the Wilcoxon test were used to distinguish the differences between the far near fields of the MCA. A value of $P < 0.05$ was regarded as statistically significant.

3. Results

One hundred fifty-eight women with a single-fetus pregnancy were enrolled in the study. Twenty-eight subjects were not able to complete the study because of an inappropriate

Table 1. Maternal, prenatal characteristics and Doppler parameters (n = 130).

Characteristic	Value
Maternal age	27.5 (23-32)
Gravida	2 (1-3)
Parity	1 (0-2)
Gestational age at the exam (weeks)	33.5 (30-36)
≤ 28	28 (21.5%)
29-34	49 (37.6%)
35-39	53 (40.9%)
BMI (kg/m ²)	27.4 (24.6-30.8)
Normal weight	45 (34.6%)
Overweight	45 (34.6%)
Class 1 obese	27 (20.8%)
Class 2 obese	13 (10%)
UA S/D	2.50 (2.16-2.97)
UA PI	0.92 (± 0.18)
UA PI percentile	41.5 (9-74)
Pregnancies unable to complete the Doppler study (n = 28)	
Inappropriate fetal presentation	3 (10.7%)
Movement of the fetus	10 (35.7%)
Abdominal subcutaneous fat thickness	15 (53.6%)

Data expressed as mean ± standard deviation or median (IQR-interquartile range Q₁-Q₃) or n (%). BMI body mass index, UA umbilical artery, S/D systole/diastole, PI pulsatility index.

Table 2. Comparison Between Mean Middle Cerebral Artery PI and PSV from Near and Far-field.

Measurement	Mean ± SD Or Median (IQR)	SEM	Mean Difference	SE Difference	t	df	P
Near-field PSV cm/s	49.83 ± 16.19	1.42	2.35	1.11	2.12	129	0.03 [‡]
Far-field PSV cm/s	52.19 ± 15.20	1.33					
Near-field PSV MoM	1.04 (1.28-0.86)						0.01 [§]
Far-field PSV MoM	1.13 (1.28-0.95)						
Near-field PI	1.78 ± 0.41	0.03	0.01	0.03	0.31	129	0.75 [‡]
Far-field PI	1.77 ± 0.4	0.03					

[‡]Paired *t*-test, [§]Wilcoxon signed ranks test. PSV Peak systolic velocity, PI pulsatility index, MoM Multiple of the median.

fetal position, movement of the fetus, or maternal abdominal subcutaneous fat thickness. Percentages regarding these incomplete studies are presented in Table 1 along with the characteristics of these subjects.

The Doppler ultrasound measurements are shown in Table 2. A notable difference was detected between the near and far-field MCA PSV (*P* = 0.03). However, no significant difference between the near-and far-field MCA S/D, PI, or RI was detected.

Additionally, we categorized the subjects according to the World Health Organisation's body mass index (BMI) classification [16] and found that the difference in MCA PSV in the normal-weight group was statistically significant (*P* = 0.009) (Table 3). However, no statistically significant difference was observed between the near and far fields of MCA PSV and PI in subjects with a BMI > 25. Furthermore, there was no significant difference in MCA S/D, RI and PI between the groups.

4. Discussion

The results of this study propose that there is no statistically significant difference between the near and far fields of the proximal portion of MCA in S/D, RI and PI. However, we found a statistically significant difference between the two sides in PSV values; to our knowledge, this is the first time this has been recognized in the field.

Fetal MCA Doppler assessment plays an increasingly important role in the management of fetuses with intrauterine growth restriction and fetal anemia [4, 17]. Karlsen *et al.* have shown that there is an association between low MCA PI and CPR, with several adverse perinatal outcomes in a high-risk population [18]. This high-risk population was defined as fetuses with a risk of growth restriction and having an umbilical artery PI > 95th percentile. Thus the impact of CPR is limited only in the management of the fetuses suffering from fetal growth restriction (FGR). Reduced CPR has been associated with abnormal fetal growth velocity, increased risk for

Table 3. Comparison Between Mean Difference of Middle Cerebral Artery PI and PSV from Near and Far Field Concerning BMI and Gestational weeks.

		Mean \pm SD or Median (IQR)	P
BMI	Normal weight		
	Near-Far field PSV cm/s	4.23 \pm 10.41	0.009 [‡]
	Near-Far field PI	0.02 \pm 0.41	0.66 [‡]
	Overweight		
	Near-Far field PSV cm/s	0.80 \pm 13.95	0.96 [‡]
	Near-Far field PI	0.01 \pm 0.36	0.89 [‡]
	Obesity Class 1		
	Near-Far field PSV cm/s	3.91 \pm 10.82	0.71 [‡]
	Near-Far field PI	0.03 \pm 0.32	0.77 [‡]
	Obesity Class 2		
	Near-Far field PSV cm/s	0.87 (5.44-15.16)	0.60 [‡]
	Near-Far field PI	0.17 (0.07-0.49)	0.34 [‡]
	≤ 28 weeks		
	Near-Far field PSV cm/s	1.74 \pm 9.41	0.31 [‡]
	Near-Far field PI	0.06 \pm 0.39	0.26 [‡]
Gestational Weeks	29-34 weeks		
	Near-Far field PSV cm/s	3.10 \pm 12.03	0.05 [‡]
	Near-Far field PI	0.06 \pm 0.33	0.18 [‡]
	35-39 weeks		
	Near-Far field PSV cm/s	1.99 \pm 14.76	0.93 [‡]
	Near-Far field PI	0.00 \pm 0.39	0.15 [‡]

[‡]Paired *t*-test, [‡]Wilcoxon signed ranks test. Data expressed as mean \pm standard deviation or median (IQR-interquartile range Q₁-Q₃). BMI body mass index, PSV peak systolic velocity, PI pulsatility index.

neonatal intensive care unit admission, and urgent cesarean delivery for fetal distress after 37 weeks; however, these risks apply only to the fetal growth restricted fetuses group, and not for non-complicated pregnancies [9].

Present evidence on abnormal CPR does not support intervening in the timing of delivery for preterm growth-restricted fetuses; and for now CPR only has a considerable impact in the management of term fetuses with FGR [19, 20]. Nevertheless, many clinicians wish to use CPR to predict term uncomplicated pregnancies. Two renowned studies stated that CPR does not have a substantial effect on adverse perinatal results in uncomplicated term pregnancies [21, 22]. There is increased interest in using CPR as a combined factor to predict the adverse outcome for uncomplicated pregnancies [23]. This increased interest for MCA should be supported by accurate measurement of MCA PI.

Although MCA Doppler assessment is essential in the management of fetal growth restriction, only one study to our knowledge has investigated the accurate assessment of MCA PI in the near or far fields of the artery. According to Salvi *et al.*, the near field of the MCA PI and PSV was not statistically significantly different from far-field MCA, but this study included only 57 fetuses [15]. Figueras *et al.* also investigated MCA PI; however, they mainly concentrated on the proximal and distal portions of the same side, not the far side in 100 fetuses [24]. This present study, which includes 130 fetuses, is the first prospectively designed study that focuses on MCA PI on both sides. We observe no significant difference between

the near field and far field of MCA PI. As a result, we can safely assume that MCA PI measurements can be made from the far-field MCA when a situation necessitates this. Clinicians are aware that sometimes fetal position, movement, or maternal characteristics make the measurement impossible to assess from the near-field MCA. According to our data, we strongly believe that, when available, far-field MCA PI can be used safely and with confidence.

It is known that MCA PSV values are the most angle-dependent measurements. Accordingly, these values should be corrected before every measurement for accurate results [12]. Early publications that compared the near and far fields of a proximal portion of the MCA were retrospective, and measurements did not include angle correction [14, 15]. Salvi *et al.* reported that care was taken to keep the angle as close as possible to 0°. However, no angle correction was used. Furthermore, this study collected data of 7 anemic fetuses retrospectively, whereas they took the control group of 50 healthy fetuses prospectively. They found the near-field PSV slightly higher than the far-field MCA PSV, with a mean difference of 1.20 cm/s. This difference appeared to be statistically insignificant [15]. In contrast to Salvi *et al.*, we designed all elements of our study prospectively with more healthy subjects (n = 130). The mean difference between the PSV values of the two sides was 2.35 cm/s; far-field PSV was higher than the near-field. Our study is singular in that near and far-field PSV were statistically different from each other; we interpreted this difference would have a substantial effect. Having

an MCA PSV > 1.5 MoMs for gestational age is a threshold for fetal intrauterine transfusion [18]. Mari *et al.* stated that from 18 weeks to 40 weeks, approximately 1.2 cm/s for (18 weeks) to 3.2 cm/s (40 weeks) difference in PSV would change the MoM from 1.50 to 1.55 [3]. Since the MoM approach is used to determine the need for fetal blood transfusion in fetal anemia, a difference such as 2.35 cm/s could change the decision of conservative fetal surveillance to an intrauterine transfusion. Notably, when performing an analysis with MoMs for MCA PSV, there was also a difference between both sides.

PSV measurements are closely related to the insonation angle. A small but distinctive difference in PSV between two sides depends on optimal insonation angle on one side from the other. Despite great effort for angle correction, depending on the fetal position, capturing zero insonation angle on one versus another side is more likely (Fig. 1). According to our own data and that of the literature, it remains impossible to decide which side of PSV is more accurate. A future study with PSV values from both sides of MCA in anemic fetuses and simultaneous fetal blood sampling should clarify which side can be used more safely. Nevertheless, our study should help alleviate the concern of clinicians as to whether there is a difference between the sides during measurements of a Doppler exam. We predict far-field MCA PSV to be moderately higher than near-field.

The proximal, intermediate and distal portions of the MCA were previously discussed in several studies. The proximal portion of both sides, the near-and far-fields of the MCA were the most reliable and statistically different from other measurement areas, i.e. middle and distal [24, 25]. Thus, we used only the proximal portion of the MCA, which was proven to be the most reliable. MCA Doppler studies demonstrate that intra-observer variabilities are as low as 5.7%, with even lower inter-observer variabilities [24, 26]. The best inter-observer reliability has been hypothesized in proximal sites. However, it was not statistically significant from the middle or distal sites [12]. In our study, all examinations were performed by the same sonographer to ensure inter-observer reliability.

Among all scanning methods, ultrasonography is most affected by obesity; the optimal image quality decreases with increased maternal obesity and skin thickness [27, 28]. We categorized pregnant women according to their BMI and observed a significant difference in PSV values of women with an average BMI ($P = 0.009$). However, no difference was found between the near and far fields of MCA PSV, S/D, RI, or PI in patients with BMI values > 25 kg/m². This difference can be attributed to a lack of subcutaneous fat tissue between the beam and the fetal artery. It is known that sonographic visualization by ultrasound deteriorates with obesity. Obese women are more likely to be overlooked by major sonographic findings and to face serious birth defects [29]. A complete anatomic scan is challenging when BMI > 30 kg/m² [27]. While it is difficult to find a specific artery

such as MCA in obese women, Doppler exams are affected by thickened subcutaneous tissue. Doppler effect also depends on the distance between the moving object, fetal blood, the observer, and the ultrasound beam. Obesity and the attendant high subcutaneous fat layer entail lower resolution and lower penetration as well as impaired study quality. We believe that, our measurements were more accurate in women with BMI < 25 kg/m²; we lose this accuracy when BMI > 25 kg/m². Our data suggest that while sonographers can assume that far-field MCA PSV values would usually be higher than near-field MCA PSV, the difference would only be important in pregnant women with an average BMI. However, the far-field measurement loses its importance in the case of an increase in BMI class due to the patient becoming overweight or obese. We therefore conclude that clinicians may ignore the difference between the two sides when a woman has a BMI > 25 kg/m².

We further subcategorized pregnant women by their gestational week. There was no statistically significant difference in the near or far fields of MCA PSV and PI among the groups. Fetal movements and head position according to the maternal pelvis, influenced by the gestational week, are thought to have an impact on Doppler assessment, but we did not observe this impact in the present study. No previous studies have categorized MCA PSV or PI according to gestational week. To investigate the effect of advance gestational age, we divided pregnant women into three groups. We expected to observe a difference in two sides in all three groups independent from the gestational week. Twenty-eight women were not able to complete the study because of an inappropriate fetal position, movement of the fetus, or maternal abdominal subcutaneous fat thickness. Among these 28 women, 18 were pregnant between 35-39 weeks. After 35-39 weeks, the mobility of the fetal head decreases, and the fetus begins to take the position it will present at delivery, leading to image windows that are less clear [30, 31]. Although a great effort was made to overcome technical limitations of advanced gestational age, it seems that this gestational age prevents observing differences between the near-far side of PSV. Likewise, fetuses < 28 weeks were extremely mobile; avoiding fetal movement could be problematic. Nevertheless, we did not expect a difference in this group because of relatively higher amniotic indexes and earlier gestational ages.

There are several limitations to this study. A Doppler assessment of intrauterine growth-restricted fetuses and anemic fetuses could have been added, as these fetuses are thought to be the leading group of interest for MCA PSV studies. Further, while the number of fetuses in this study could be considered insufficient, no studies exceed the number of subjects used in the present one. We only made one measurement per subject; repeated measures from the same subject as the gestational weeks progress may be a more effective way to mediate the two sides of flow changes in the MCA rather than measuring different subjects at different

weeks. Finally, although we concluded that the far-field side had higher PSV values than the near-field side, we could not comment on which measurement was more accurate.

5. Conclusions

In conclusion, when making MCA PSV measurements, sonographers should be aware that a small difference can be present between the near and far fields of the artery. Yet sonographers should not spend undue time seeking the near-field MCA, as differences between the near and far fields are minute. However, clinicians can rely on both the near and far fields of the MCA when measuring MCA PI.

Abbreviations

BMI, Body Mass Index; CPR, Cerebroplacental ratio; FGR, Fetal growth restriction; ISUOG, International Society of Ultrasound in Obstetrics and Gynecology; MCA, Middle Cerebral Artery; MoM, Multiples of Median; PI, Pulsatility Index; PSV, Peak Systolic Velocity; RI, Resistance Index; S/D, Systole/diastole ratio; UA, Umbilical Artery.

Author contributions

DA: Project Development, Data Collection, Manuscript Writing; BKA: Data Collection, Data Analysis Manuscript Writing; MK: Data Collection, Manuscript Writing; HG: Data Collection, Manuscript Writing; AE: Project Development, Data Analysis, Drafting the Manuscript, Manuscript Editing.

Ethics approval and consent to participate

This prospective study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by Izmir Tepecik Research and Education Hospital's ethics committee (Date: 12/02/2019, No 2019/14-21). The clinical trial is registered to ISRCTN registry with reference number 38902. Written informed consent was obtained from all individual participants included in the study.

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Conflict of interest

The authors declare that they have no conflict of interest.

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