Assessment of the Placental Cord Insertion Using 3-Dimensional Ultrasound at the Time of the Structural Fetal Survey

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ABSTRACT

OBJECTIVES

The influence of placental morphologic characteristics on pregnancy outcomes is poorly understood. Our objective was to evaluate the relationship of the distance of the placental cord insertion from the placental edge (PCI-D) with associated placental characteristics as well as birth outcomes.

METHODS

We performed a retrospective cohort study of nulliparous women with singleton gestations undergoing obstetric ultrasound examinations between 14 and 23 weeks' gestation with a cervical length of greater than 3.0 cm who delivered between 24 and 42 weeks. A 3-dimensional volume of the placenta was evaluated. The PCI-D was obtained with Virtual Organ computer-aided analysis software (GE Healthcare, Milwaukee, WI). Generalized linear regression and generalized additive models were fitted to explore the associations between the PCI-D in relation to demographic and clinical characteristics.

RESULTS

A total of 216 pregnancies were included in the analysis. The PCI-D did not correlate with maternal age, gestational age at delivery, mode of delivery, or 5-minute Apgar score. Although not statistically significant, the birth weight *z* score (P = .09) was associated

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with a longer PCI-D, and gravidity was associated with a shorter PCI-D (P = .10). A low-lying placenta or placenta previa was associated with a longer PCI-D (P = .03).

CONCLUSIONS

The PCI-D is associated with a low placental position in the second trimester. These data are helpful for understanding placental development. The PCI-D may be associated with pregnancy-related factors such as birth weight and multigravidity. More research is required to evaluate the effects of pregnancy-related factors on the PCI-D and the effect of the PCI-D on pregnancy outcomes.

Keywords: cord insertion, low-lying placenta, obstetrics, placenta, placental development, placental structure, placenta previa, 3-dimensional ultrasound.

ABBREVIATIONS

- **3D:** 3-dimensional
- **PCI-D:** distance of the placental cord insertion from the placental edge
- **US:** ultrasound

Certain placental morphologic and cord insertion characteristics are known to be associated with adverse perinatal outcomes. Neonatal intensive care unit admission, perinatal death, and neonatal death are more common in pregnancies complicated by placenta previa.[1] A velamentous cord insertion and vasa previa are associated with preterm birth, fetal growth restriction, and perinatal death.[1] Other less widely evaluated placental and cord insertion attributes such as placental shape irregularities and vasculogenic zone deformations may also be useful in predicting pregnancy outcomes.[2] Furthermore, these placental characteristics are thought to develop[2] and be detectable[3] in early pregnancy.

Several studies have shown that a placental cord insertion located within the lower uterine segment, which is expected to have a less robust blood supply in early pregnancy, may lead to increased pregnancy complications related to abnormal placentation or to placental cord insertion development.[3], [4] Others have suggested that a nonround/oval placental shape reflects a suboptimal placental vascular network that leads to lower birth weights in those fetuses with irregularly shaped placentas.[5] The distance of the placental cord insertion from the placental edge (PCI-D) is a related characteristic that could be used to better stratify high- versus low-risk pregnancies.

In this study, we assessed the relationship between the PCI-D at the time of the fetal structural survey and other placental characteristics in relation to adverse perinatal outcomes. We hypothesized that a decreased PCI-D would be associated with adverse pregnancy outcomes. Furthermore, we sought to better understand placental development, especially of the placental cord insertion.

MATERIALS AND METHODS

This retrospective cohort study was performed at Diagnostic Ultrasound Associates, PC. Over a 10-month period, 227 consecutive nulliparous women undergoing obstetric ultrasound (US) examinations between 14 and 23 weeks' gestation with a singleton gestation and cervical length greater than 3.0 cm who delivered between 24 and 42 weeks at Brigham and Women's Hospital were included. Those whose placental cord insertions could not be evaluated (n = 8) and those with velamentous placental cord insertions

(n = 3) were excluded in the analysis. Color Doppler US was not used for identification of the placental cord insertion. The study was approved by the Institutional Review Board of Brigham and Women's Hospital.

All scans were performed with a Voluson 730 system equipped with a 4–7-MHz 3-dimensional (3D) volume transducer (GE Healthcare, Milwaukee, WI). As per our protocol for structural fetal surveys, in addition to obtaining 3D volumes of the fetus, a 3D volume of the placenta was obtained.[6] This 3D volume of the placenta was evaluated with Virtual Organ computer-aided analysis software (GE Healthcare). After viewing the placenta in the multiplanar mode, the 3D volume of the placenta was centered on the screen in the acquisition plane (A). The 3D volume was systematically evaluated, scanning through the volume from one side of the placenta to the other until the placental cord insertion could be identified. After the placental cord insertion was identified, the “marker dot” was placed on the center of the placental cord insertion, and the insertion was centered on the screen. The volume was then rotated 360° until the shortest distance between the placental edge and the placental cord insertion was identified. The marker dot was then placed at the vessel edge bordering the closest placental edge, and the distance was measured. The PCI-D was then obtained with the embedded measurement tool in the Virtual Organ computer-aided analysis software (Figure [1]). Those with marginal placental cord insertions were assigned a distance of 0.0 cm from the placental edge, and the remainder of cases were measured to 1 decimal place in centimeters from the nearest placental edge (Figure [2]). Velamentous placental cord insertions were classified as those that were fully inserted into the fetal membranes and were distinct from marginal placental cord insertions whose insertions involved the placental margin.

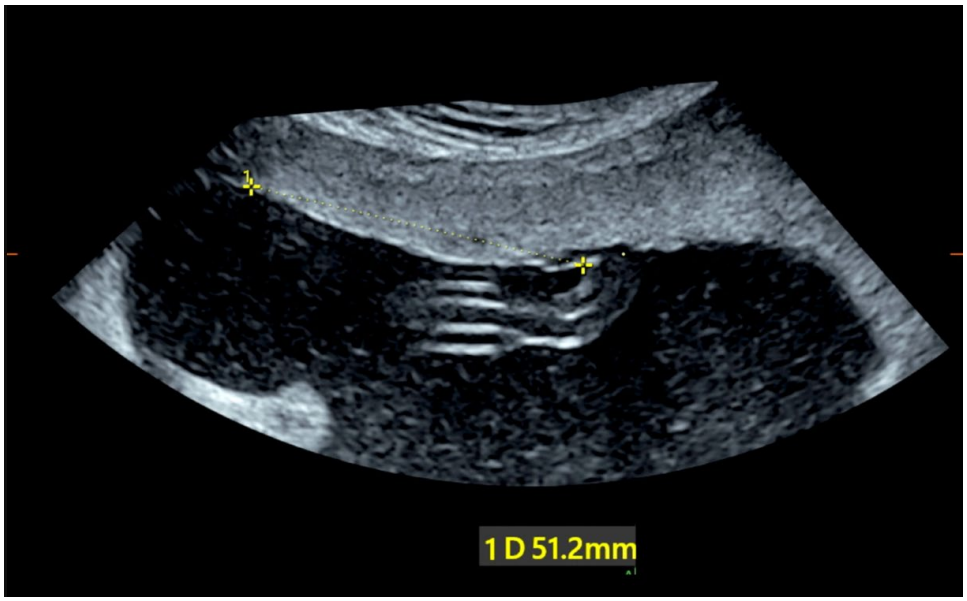

Figure 1: Three-dimensional volume of an anterior placenta showing the marker dot used in the center of the placental cord insertion and the measurement of the placental cord insertion from the placental margin (calipers).

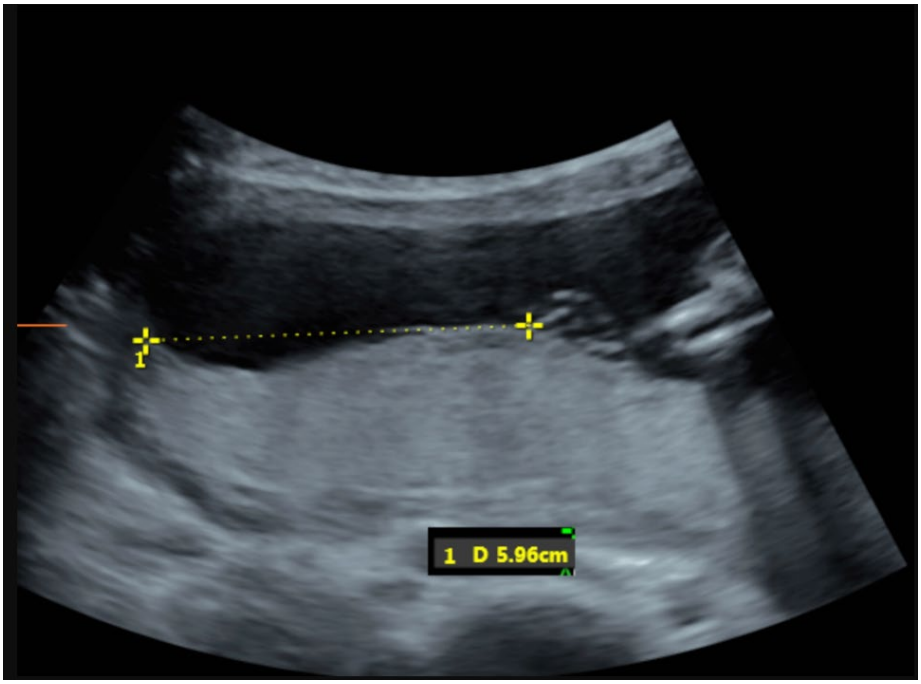

Figure 2: Three-dimensional volume of a posterior placenta showing the measurement of the placental cord insertion from the placental margin (calipers).

Demographic, US, and pregnancy outcome information was abstracted from the medical record. Analyses were performed with SAS version 9.4 software (SAS Institute Inc, Cary, NC). $P < .05$ was used to define statistical significance. Generalized linear regression and generalized additive models were fitted to explore the associations between the PCI-D in relation to demographic and clinical characteristics. Confounding variables were selected on the basis of an a priori review of the literature (maternal age and gestational age at US) as well as based on univariate statistical significance ($P < .10$). We additionally performed a sensitivity analysis restricted to those participants that underwent a Cesarean delivery.

RESULTS

The cohort included 227 patients for whom 3D placental volumes were obtained. Eleven patients were excluded from the analysis, including 8 (3.5%) patients for whom the 3D volume did not contain adequate visualization of the placental cord insertion and 3 (1.3%) patients who had a velamentous placental cord insertion. This left a study population consisting of 216 patients. Maternal demographic, delivery, and placental data are summarized in Table 1. The mean gestational age at delivery was 39.3 weeks, and the mean maternal age at delivery was 31.4 years. In total, 21.3% of our cohort were 35 years of age or older at the time of delivery. The cesarean delivery rate was 39.4%, with approximately one-third of cesarean deliveries performed for a nonreassuring fetal status; 32.9% of study participants underwent inductions of labor; of these, 45.8% were executed for postdates, and 20.8% were indicated for hypertension. The mean birth weight was 3340 g, and 97.7% of neonates had a 5-minute Apgar score of 7 or higher.

Table 1. Basic Demographics and US Characteristics

Variable	n	Value
Maternal age at delivery, y	216	31.4 ± 4.6 (16–42)
≤34, %	170	78.7
>34, %	46	21.3

Gravidity	216	
>1		40 (18.5)
>2		15 (6.9)
Gestational age at delivery, wk	216	39.3 ± 2.1 (26.6–42.6)
Preterm birth (<37 wk)	216	19 (8.8)
Mode of delivery		
Vaginal (spontaneous and surgical)		131 (60.6)
Cesarean		85 (39.4)
Cesarean indication		
Nonreassuring fetal status		27 (31.8)
Other		58 (68.2)
Induction		
Yes		71 (32.9)
No		145 (67.1)
Indication for induction		
Hypertension		15 (20.8)
Postdates		33 (45.8)
Other		24 (33.3)
Birth weight, g	216	3340 ± 612 (1021–4479)
Birth weight by gestational age *z* score	216	–0.14 ± 0.96 (–2.50–1.81)
Gestational age at delivery, wk	216	39.4 ± 1.9 (26.6–42.6)

Female	207	111 (53.6)
5-min Apgar <7	216	5 (2.3)
Gestational age at scan, wk	216	18.3 ± 1.2 (14.0–23.0)
Cervical length at time of scan, cm	215	3.77 ± 0.51 (3.0–5.4)
Placental location	216	
Anterior		95 (44.0)
Posterior		73 (33.8)
Lateral		6 (2.8)
Fundal		10 (4.6)
Low-lying or previa		32 (14.8)
Placental cord insertion distance from placental edge, cm	216	2.79 ± 1.24 (0–6.0)
Cord insertion	216	
Normal (>0.0)		204 (94.4)
Marginal (0.0)		12 (5.6)

Data are presented as mean ± SD (range) and number (percent) where applicable.

The mean gestational age at which the US study was completed was 18.3 weeks, ranging from 14.0–23.0 weeks. Regarding placental location, 44% of placentas were classified as anterior, 34% as posterior, and 7% as fundal or lateral. A low-lying placenta or placenta previa was diagnosed in 14.8% of study participants; all had resolved by the time of delivery.

The relationship between the PCI-D and selected demographic, US, and pregnancy outcome information is shown in Tables 2 and 3. In bivariate linear regression models, an increased PCI-D was associated with an increased birth weight z score (P = .04), and a decreased PCI-D was associated with gravidity of more than 1 (P = .03). When adjusted for maternal age, gestational age at US, gravidity, birth weight, and 5-minute Apgar score lower than 7, having a low-lying placenta or placenta previa was associated with a 0.52 (95% confidence interval, 0.06, 0.98) increase in the PCI-D. In the sensitivity analysis, those participants who underwent a cesarean delivery (Table 4) had a decrease in the PCI-D associated with increased maternal age (P = .004) and an increase in the PCI-D associated with an increase in the birth weight z score (P = .02).

Table 2. Crude Generalized Linear Regression Models

Variable	**n**	**β (95% CI)**	***P***
Maternal age (continuous)	216	–0.03 (–0.07, 0.01)	.11
Maternal age	216		
≤34 y		Reference	
>34 y		–0.22 (–0.62, 0.19)	.30
Gestational age at delivery	216	0.02 (–0.06, 0.10)	.61
Preterm birth	216	0.12 (–0.46, 0.71)	.68
Gestational age at US	216	0.08 (–0.05, 0.22)	.22
Birth weight (*z* score)	216	0.18 (0.01, 0.35)	.04
5-min Apgar <7	216	0.98 (–0.12, 2.07)	.08
Cervical length	216	0.37 (–0.87, 1.61)	.56
Gravidity			
>1	216	–0.46 (–0.88, –0.04)	.03

>2	216	–0.31 (–0.97, 0.34)	.34
Female fetus	216	–0.11 (–0.45, 0.23)	.54
Induction	216	0.01 (–0.35, 0.36)	.97
Mode of delivery	216		
Spontaneous/surgical vaginal		Reference	
Cesarean		0.23 (–0.11, 0.57)	.19
Placental position	216		
Posterior		–0.19 (–0.57, 0.19)	.32
Fundal		–0.23 (–1.03, 0.58)	.58
Lateral		–0.15 (–1.17, 0.87)	.78
Low-lying or previa		0.47 (–0.03, 0.96)	.07

CI indicates confidence interval.

Table 4. Adjusted Linear Regression Model: Cesarean Deliveries Only (n = 85)

Variable	**β (95% CI)**	***P***
Maternal age	–0.08 (–0.13, –0.03)	.004
Gestational age at US		
<18.0 wk (n = 37)	Reference	
≥18.0 wk (n = 48)	0.45 (–0.09, 0.99)	.10
Birth weight (*z* score)	0.30 (0.04, 0.56)	.02
Placental position (low-lying or previa)	0.27 (–0.49, 1.03)	.49
Nonreassuring fetal status indication for cesarean	0.40 (–0.21, 1.00)	.20

- CI indicates confidence interval.

DISCUSSION

The placenta has an inadequately understood influence on perinatal outcomes. Furthermore, the relative importance of placental morphologic characteristics as a determinant of birth outcomes is not reflected in the quantity of literature that is available to help guide management during pregnancy. A recent meta-analysis found a lack of standardization in definitions of an abnormal placental cord insertion to be a major limitation; nonetheless, the authors found an association of an abnormal placental cord insertion with emergent cesarean delivery.[7] If certain placental characteristics that are known to be associated with adverse pregnancy outcomes are identified and definitions standardized, they could be used to inform antepartum management of these pregnancies, beginning with a routine antenatal systematic evaluation of the placental structure such as the placental cord insertion and placental shape.

In our study, we found that the PCI-D was associated with the placental position at the time of the structural fetal survey. We also identified a trend toward increased birth weight as the PCI-D increased. This trend fits with existing data suggesting that placentas with noncentral umbilical cord insertions are less efficient than those in which the placental cord insertion is centrally located.[8] The importance of the trend toward a shorter PCI-D in multigravidas is unclear and should be further explored.

The positive association between the PCI-D and a low-lying placenta or placenta previa in the second trimester requires further discussion. All of the low-lying placentas in our population resolved by the time of delivery. The longer PCI-D among these pregnancies, which were low lying in the second trimester yet ultimately resolved, suggests that these pregnancies may vary from those with a shorter PCI-D. These pregnancies with more centrally located cord insertions would be expected to be more efficient[8] and, for this or other reasons, may have been associated with resolution of their low-lying position by the time of delivery. This finding is in concert with the findings of Hasegawa et al.,[3] who documented that the risk of abnormal placentation was higher with those low-lying

placentas that did not resolve over gestation. Our finding that resolution of the low-lying placentas was associated with a more centrally located placental cord insertions suggests that these placentas are less likely to be associated with abnormal placentation, although the exact mechanism remains elusive. To better understand placental development and to optimize obstetric outcomes, it is vital to follow placental cord insertion development through gestation, as abnormal placental cord insertions can be associated with membranous vessels and their potential sequelae, as can be seen with vasa previa.[9] Hasegawa et al[4] also showed that there was an excellent correlation between first- and second-trimester placental cord insertion distances from the internal cervical os. Further research into placental and placental cord insertion development and their associated adverse sequelae throughout gestation could provide valuable data for optimizing patient care.

The current competing theories of placental cord insertion development are trophotropism with placental “migration” during gestation toward more highly vascular areas of the uterus, with resultant abnormal placental cord insertion development, and abnormal primary implantation (polarity theory), whereby the blastocyst obliquely implants in the uterus, leading to early development of abnormal placental vasculature.[10] Although our study does not specifically refute or support either theory of placental cord insertion development, our identification of placental migration during resolution of a low-lying placenta or placenta previa does suggest more influence of trophotropism on placental development. Better elucidation of the specifics of the placental cord insertion in the first trimester and longitudinal data from the first trimester to the third trimester would help clarify the development of the placenta and, more specifically, of the placental cord insertion and perhaps would suggest a novel single unifying theory of placental cord insertion development.

Because of the known association between placental cord insertion abnormalities and poor obstetric outcomes, specifically emergency cesarean delivery, we chose to do a sensitivity analysis of those undergoing cesarean deliveries only, since approximately one-third of the cesarean deliveries were indicated for a nonreassuring fetal status. The trend seen in the raw data in which maternal age trended with a shorter PCI-D became

statistically significant in women who had cesarean deliveries. It could be speculated that the ability of the uterus of older gravidas to facilitate uniform growth of the placenta may be decreased compared to that of younger gravidas, thus leading to a decreased PCI-D in these placentas. The association between the birth weight *z* score and longer PCI-D became statistically significant in this group, which fits well with the suggestion of improved placental efficiency with more central placental cord insertions.[8] The fact that we did not find an association between a nonreassuring fetal status (as the indication for cesarean delivery) and the PCI-D could have been due to our low numbers in this subanalysis.

Our study was not without limitations and must be interpreted within the context of its design. Our sample was a convenience sample, in which 3D volumes were retrospectively evaluated for nulliparous women after they underwent scheduled prenatal US examinations. This factor may decrease the generalizability of our findings. Furthermore, our study was limited by the relatively small number of participants, which makes adjusting for confounding factors difficult. Although the trend in the association between increased birth weight and an increased PCI-D is biologically plausible, it could be the result of confounding factors for which we were unable to control, given our sample.

A major strength of this study was its single-center design, with all US examinations being performed and read by sonologists experienced in fetal US. Our study also contributes to the relatively sparse literature on the effect of the placental form on common obstetric outcomes. Most placental cord insertions can be readily identified with 2-dimensional US, and the use of 3D technology was chosen for better clarification of placental development and not as a requirement, recommendation, or even preference for incorporating 3D US into the US visualization of the placental cord insertion. It is unclear whether our identification rate for placental cord insertions could have been improved with the use of color Doppler US. Although not the purview of this study, color Doppler US can aid in the identification of other placental and cord abnormalities such as velamentous cord insertions and vasa previa.

More studies are needed to better parse out the specific placental characteristics that may place a pregnancy at risk of an adverse event, as well as the process of placental

development that leads to these characteristics. Specifically, more research is needed to evaluate the effects of pregnancy-related factors on the PCI-D and the effect of the PCI-D on pregnancy outcomes. Further exploration of placental development and the specific influence of the placental location on the development of the placental cord insertion would assist with our understanding of abnormal placentation. Identification of specific risk factors for abnormal placentation, or the early identification thereof, could then inform antenatal testing and possibly delivery timing decisions to prevent adverse outcomes from occurring.

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