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REVIEW

WILEY

Assessment of pericallosal artery at 11–14 weeks of gestation: Cohort study and meta-analysis

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Abstract

Objectives: To report the rate of visualization of the pericallosal artery (PCA) in the first trimester of pregnancy (11–14 weeks).

Methods: Prospective observational study of consecutive fetuses undergoing first trimester risk assessment for chromosomal anomalies. The presence of PCA was assessed in a midsagittal view of fetal brain using high-definition power Color Doppler. A normal course of the PCA was defined as the visualization of an artery emerging from the anterior cerebral artery running parallel the corpus callosum (CC). The reference standard was the visualization of CC and PCA between the 20 and 22 weeks of gestation. We also performed a systematic review and meta-analysis of the published literature. Multivariate logistic regression and random-effect meta-analyses of proportion were used to analyze the data.

Results: Cohort study: Five-hundred women were included. PCA was identified trans-abdominally or transvaginally at 11–14 weeks of gestation in 98.8% (95% CI 97.4–99.6: 494/500); of the four cases of PCA not identified one had a diagnosis of complete agenesis of the corpus callosum during the anomaly scan which was confirmed at birth.

Systematic review of the published literature: Six studies (1093 fetuses, including the present series) were included. The PCA was detected at the 11–14 weeks scan and confirmed to co-exist with a normal CC at time of the anomaly scan in 96.9% (95% CI 93.8–99.0); 20.6% (95% CI 5.7–41.7) of fetuses with no clear identification of the PCA at the 11–14 weeks scan had a normal appearance of the CC at the time of anomaly scan.

Conclusion: Prenatal ultrasonography has a high diagnostic accuracy in detecting PCA in the first trimester. Visualization of the PCA at the time of 11–14 scan is highly specific for the presence of a normal CC later in pregnancy.

KEYWORDS
corpus callosum, first trimester, pericallosal artery, ultrasound

1 | INTRODUCTION

Agenesis of the corpus callosum (ACC) is among the most common central nervous system anomalies detected prenatally. Prenatal identification of fetuses with ACC is crucial in view of its association with abnormal neurodevelopmental outcome, mainly involving motor control, coordination, language, and cognitive status.[1]

Prenatal diagnosis of ACC requires a sagittal view of the fetal brain to demonstrate the absence of the corpus callosum (CC), which commonly appears as a thin anechoic space, lined superiorly and inferiorly by two echogenic lines. Use of color Doppler may improve diagnosis demonstrating the loss of the semicircular loop of the pericallosal artery (PCA). However, a sagittal view of the fatal brain is not required for the routine standard assessment of fetal brain and ACC is commonly suspected by several indirect signs detected at the axial view of the brain, including absence of the cavum septi pellucidi, displaced frontal horns, widened interhemispheric fissure, and colpocephaly.[2,3]

Several recent studies reported that the prenatal diagnosis of ACC can be suspected at 11–14 weeks of gestation by identifying an abnormal course of the PCA. However, the small sample size of these studies, differences in type and time at ultrasound assessment as well as the inclusion criteria impair our ability to extrapolate robust evidence on the actual diagnostic performance of first trimester ultrasound in detecting CC abnormalities in the first trimester of pregnancy.[4–8]

The primary aim of the study was to report the rate of visualization of the PCA using ultrasound in a large cohort of consecutive pregnancies at 11–14 weeks. The secondary aim was to conduct a systematic review reporting the overall visualization of PCA in the published literature.

2 | MATERIAL AND METHODS

2.1 | Cohort study

This was a prospective cohort study including consecutive women attending the 11–14 weeks scan in two large fetal medicine referral centers in Italy. All consecutive women undergoing first trimester risk assessment for chromosomal anomalies were included. Twin pregnancies, those with suspected fetal anomalies or increased nuchal translucency were excluded. All women gave their written informed consent, and the study was approved by the local ethical committees.

The primary outcome of the study was the rate of visualization of PCA using high-definition Doppler. A normal course of the PCA was defined as the visualization of an artery emerging from the distal part of the anterior cerebral artery and coursing over the superior surface of the body of the CC (Figure 1). The reference standard was the visualization of the corpus callosum and PCA in the second trimester of pregnancy, at the time of the routine anomaly scan for fetal anomalies, between the 20 and 22 weeks of gestation. All ultrasound examinations were performed using Samsung Hera W10 Ultrasound machine (Samsung Healthcare, Seoul, South Korea). Assessment of the PCA was carried out using MV-Flow, a high-definition Power

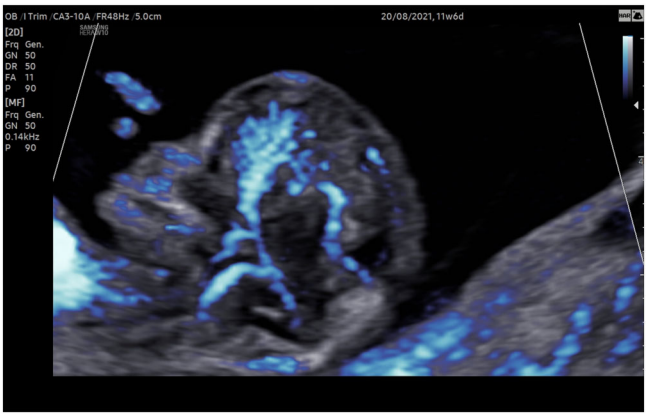

FIGURE 1 Ultrasound visualization of PCA in the first trimester of pregnancy in a mid-sagittal view of the fetal brain. The PCA emerges from the distal portion of the anterior cerebral artery and courses over the superior surface of the body of the CC in the pericallosal cistern

Color Doppler tool which offers a detailed view of low-velocity blood flow in relation to the surrounding tissues, with high sensitivity and resolution.

In order to identify PCA, a mid-sagittal view of the fetal brain was acquired and magnified; then high-definition Doppler with a color box limited to the fetal head, a low pulse repetition frequency, low filter and moderate color gain, was applied. In case PCA was not visualized with trans-abdominal ultrasound, a trans-vaginal scan was performed. All the examinations were performed by experienced investigators certified by the Fetal Medicine Foundation observing safety procedures including the ALARA principle.[9,10]

Continuous variables were reported as mean (and standard deviations), while categorical data as proportions with their 95% confidence intervals (CI). Results were reported as proportions with their 95% confidence intervals (CI). Categorical variables were compared using chi-squared test. Furthermore, we planned to run multivariate logistic regression analysis to investigate those factors (if any) which were independently associated with the non-visualization of PCA at the time of the 11–14 weeks scan. For the purpose of this analysis the following co-variates were included in the regression model: maternal age, body mass index, gestational age at ultrasound, prior cesarean section or uterine surgery, and the placental position. Statistical analysis was performed using SPSS Statistics for Windows, Version 27.0. (SPSS, Armonk, NY: IBM Corp). A p-value <0.05 was considered as statistically significant.

2.2 | Systematic review and meta-analysis

The literature review was performed according to an a-priori designed protocol, following Prisma guidelines.[11–15] MEDLINE, Embase, CINAHL, and Google Scholar databases were searched, utilizing combinations of the relevant medical subject heading (MeSH) terms, key words, and word variants for "corpus callosum" and "ultrasound." The search and selection criteria were restricted to English language.

TABLE 1 General characteristics of the included studies

Authors	Year	Country	Study design	Period considered	Inclusion of cases with abnormal NT or anomalies	Ultrasound assessment	Reference standard	Fetuses (*n*)
Present study	2021	Italy	Prospective	2021	No	TA/TV	2nd trimester US	500
De Keersmaecker et al.	2017	Belgium	Prospective	ns	No	TA	2nd trimester US	15
Kalaycı et al.	2017	Turkey	Restrospective study	2014–2015	Yes	TA	2nd and 3rd trimester US	278
Diaz-Guerrero et al.	2013	Venezuela	Retrospective	ns	Yes	NS	2nd trimester US	150
Conturso et al.	2013	Italy	Prospective	2013	No	TA	2nd trimester US	70
Pati et al.	2011	Italy	Retrospective	ns	Yes	TA/TV	2nd and 3rd trimester US	80

We included studies reporting the assessment of PCA during the 11–14 weeks scan. The main outcome measure was the visualization of a normal PCA.

Only studies reporting the detection rate of PCA or CC at 11–14 weeks were included in the analysis. Studies on second trimester or those from which gestational age at assessment could not be extrapolated were excluded. Studies published before 2000 and those reporting less than three cases were also excluded to avoid publication bias.

Two reviewers (RDG, SA) independently extracted data. Inconsistencies were discussed among the reviewers and consensus reached.

Quality assessment of the included studies was performed using the Newcastle–Ottawa Scale (NOS) for cohort studies.[16] Random-effect meta-analyses of proportions were used to analyze the data.[17] All analyses were carried out using StatDirect (StatsDirect statistical software. http://www.statsdirect.com. England: StatsDirect Ltd. 2013).

3 | RESULTS

3.1 | Cohort study

Five-hundred women were included in the analysis. Mean maternal age at the assessment was 31 ± 2.3 years, while mean BMI was 27.1 ± 2.8. Mean gestational age at scan was 12.2 ± 0.7 weeks; placental position was anterior in 58.6% (54.1–63.0; 293/500) of women, while 17.8% (95% CI 14.5–21.4; 89/500) had a prior Cesarean section. PCA was identified trans-abdominally at the time of the 11–14 weeks scan in 98.8% (95% CI 97.4–99.6: 494/500); of the four cases of PCA not identified in the first trimester with trans-abdominal ultrasound, one was detected with trans-vaginal scan, two were identified at 16 and 17 weeks of gestation respectively while the latter had a diagnosis of complete ACC at the time of the anomaly scan which was also confirmed at birth. All these women had high BMI (>35). In all cases in which PCA was identified in the first trimester, the presence of this vessel.

Logistic regression analysis was not performed as the numbers in the group with no visualization of the PCA were insufficient for meaningful analysis.

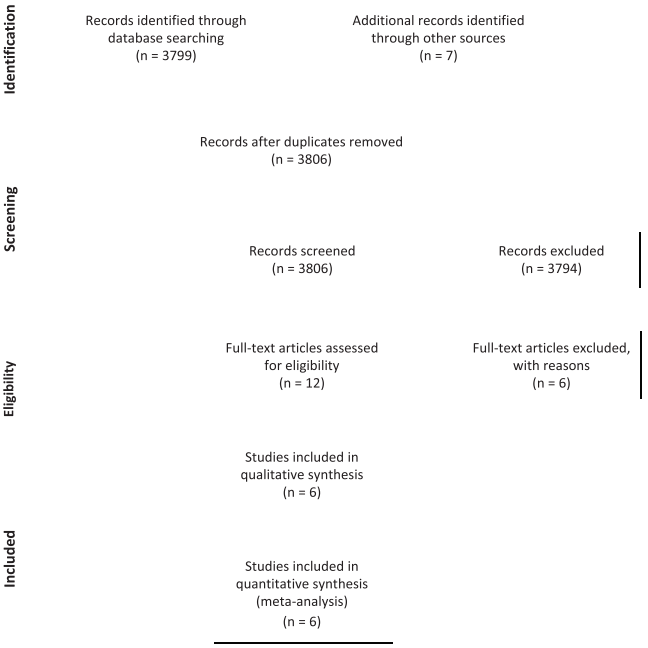

FIGURE 2 Systematic review flow-chart

TABLE 2 Quality assessment of the included studies according to Newcastle-Ottawa Scale (NOS) for cohort study

Authors	Year	Selection	Comparability	Outcome
De Keersmaecker et al.	2017	★★★	★	★★
Kalaycı et al.	2017	★★	★	★★
Diaz-Guerrero et al.	2013	★★	★	★★
Conturso et al.	2013	★★	★	★★

Note: According to NOS, a study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.

3.2 | Systematic review of the published literature

Six studies (including the present series)[4–8] were included in the systematic review (Table 1, Figure 2). These studies included 1093

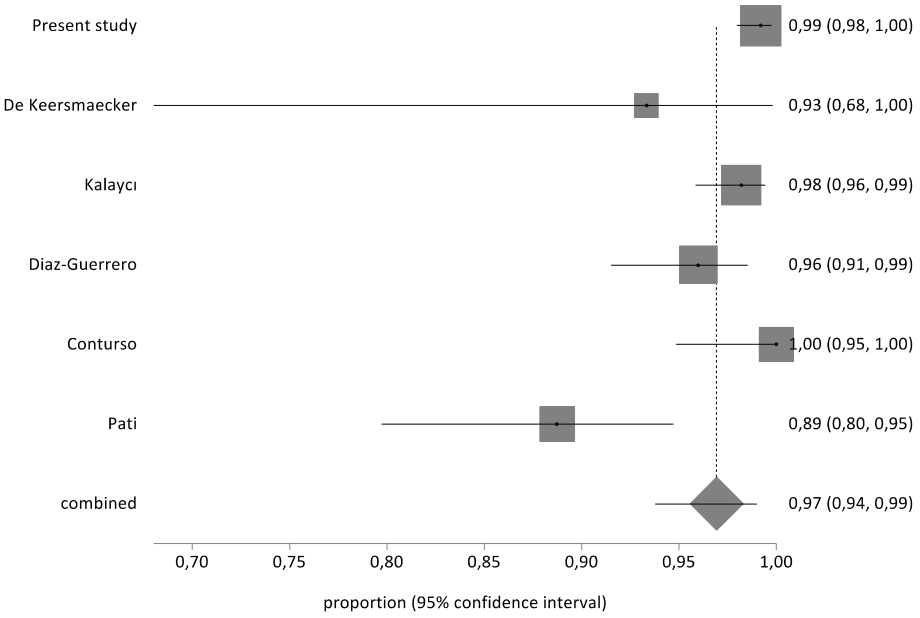

FIGURE 3 Pooled proportions for the rate of visualization of PCA at the 11–14 weeks scan

fetuses undergoing PCA assessment at the time of the 11–14 weeks scan.

Quality assessment based on NOS guidelines is shown in Table 2. Most of the studies were of moderate quality, and there was a low risk of bias and low concern regarding the applicability of the studies.

Overall, the PCA was detected at the 11–14 weeks scan and confirmed to co-exist with a normal CC later at the anomaly scan in 96.9% (95% CI 93.8–99.0, I^2: 79%, 1068/1093, six studies) (Figure 3). Conversely, 20.6% (95% CI 5.7–41.7, I^2: 0%; 3/15, five studies) of fetuses with no identification of the PCA at the time of the 11–14 weeks scan had a normal appearance of the CC at the time of anomaly scan or at birth.

4 | DISCUSSION

The findings from this cohort study and systematic review show that assessment of the PCA in the first trimester of pregnancy is feasible and accurate in most cases. Of those fetuses with lack of normal appearance of the PCA, the majority showed a normal appearance of the CC. The findings from the systematic review were in line with those of the cohort study, confirming the high diagnostic performance of first trimester ultrasound in detecting PCA and CC.

This is the largest series exploring the diagnostic performance of prenatal ultrasound in identifying the PCA in the first trimester of pregnancy. The strengths of the study were its prospective design, relatively large sample size and inclusion of fetuses with no suspected structural anomalies or increased NT. The small number of cases in some of the included studies and their retrospective design were the main limitations of the systematic review. Some studies considered fetuses with increased NT, chromosomal anomalies, or structural malformation. Furthermore, all ultrasound scans were performed by experienced operators, thus questioning about the actual performance of first trimester ultrasound in detecting PCA when performed by less experienced physicians. Finally, we could not perform meaningful subgroup analyses according to the operator's experience or gestational age at assessment.

Anomalies of the fetal CC are among the most common CNS malformation detected at the time of the routine anomaly scan. Acquisition of a midsagittal view of the fetal brain demonstrating the absence of the CC is crucial in identifying ACC. Use of color Doppler may improve the diagnosis demonstrating that the course of artery (PCA is lost, and this may be particularly useful in case of unfavorable fetal position or in case assessment of the midline structures may be impaired by maternal factors, such as raised BMI.[18,19]

Advances in prenatal imaging techniques in the last decade has allowed a more detailed assessment of fetal anatomy in early gestation, leading to an increased number of studies reporting the feasibility of early prenatal diagnosis of CNS anomalies in the first trimester of pregnancy. Most anomalies involving fetal brain are obviously present since the first trimester of pregnancy. Despite that the overall reported detection rate of CNS anomalies during the first trimester of pregnancy is low.[19,20] The International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) currently recommends that the fetal head structures that should be visualized in the first trimester of pregnancy include the cranial bones, the midline falx and the choroid-plexus-filled ventricles. This approach allows identification only of the most common anomalies involving the cranial bones and interhemispheric fissure, such as holoprosencephaly and acrania.[1,2] Anomalies involving the CC are associated with significant rearrangement of the fetal neuroanatomy, including a widened interhemispheric fissure, colpocephaly or displaced frontal horns, which are not even easily detected in the midtrimester of pregnancy. In this scenario, identification of PCA may help in suspecting these anomalies.[3] Furthermore, acquisition of a midsagittal view of the fetal brain is relatively easy in the first trimester of pregnancy because it

represents the imaging plane used to measure the NT. Assessment of the PCA with high-definition color Doppler represent another feasible and reproducible approach to indirectly detect CC in the first trimester of pregnancy and may help in more accurately describing the fetal anatomy in those cases with suspicion of fetal structural or chromosomal anomalies, or to reassure parents with a prior pregnancy complicated by fetal ACC.[4–8,21,22]

5 | CONCLUSION

Prenatal ultrasound has a high diagnostic accuracy in detecting PCA in the first trimester. Visualization of the PCA at the time of 11–14 weeks ultrasound scan is highly specific for the presence of a normal CC later in pregnancy.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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