ORIGINAL ARTICLE

4D Sonography in Prenatal Diagnosis of Fatal Anomalies

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Abstract

Background: ***Although routine scanning is increasingly being offered during the first trimester, especially in high-resource countries, routine ultrasound examination is still most typically conducted in the second trimester if resources and access are available as part of prenatal care.***

Aim and objectives: ***To compare the efficacy of 2D and 4D ultrasonography in the assessment and diagnosis of congenital abnormalities in the developing foetus throughout the first and second trimesters of pregnancy.***

Subjects and methods: ***From November 2023 through November 2024, the radiodiagnosis department at Al-Hussein hospital, Al-Azhar University, conducted a cross-sectional study on 200 pregnant women at high risk during the first and second trimesters.***

Results: ***Fifty pregnant women were evaluated using 2D and 4D ultrasound scans, and 52 abnormalities were found. In 13% of cases, 4D-US outperforms 2D-US; in 30%, the results are similar; and in 17% of cases, there is less information. Only in cases of specific facial and limb abnormalities was 4D-US useful.***

Conclusion: ***The findings underscore the added diagnostic value of 4D-US in prenatal screening, particularly in high-risk pregnancies. While 2D-US remains the primary screening modality, the superior sensitivity and specificity of 4D-US support its role as an adjunctive imaging tool, enhancing early detection and improving perinatal outcomes.***

Keywords: Fetal anomalies; 4D-Sonography;Prenatal diagnosis

1. Introduction

Accurate information that has allowed the delivery of improved prenatal care with the greatest potential outcomes for mother and fetus is the primary goal of a foetal ultrasound anomaly scan employing 4D-ultrasonography. During the first trimester of pregnancy, it is crucial to check the baby's viability, precisely estimate the gestational age, count the fetuses, and evaluate the chorionicity and amnioticity of any multiple pregnancies. At the conclusion of the first trimester, the scan can also assess the nuchal translucency thickness (NT) and identify obvious fetal abnormalities in health systems that provide screening for aneuploidy in the first trimester.[1]

For fetal anatomical examination in both low-risk and high-risk pregnancies, the standard of care is the second-trimester '18-22-week' scan. With the development of reliable transvaginal probes in the late 80s and early 90s, it became possible to assess the foetal anatomy and identify abnormalities during the first trimester.[2]

Early anatomy scanning is gaining popularity again thanks to the 11–13 week window for NT aneuploidy screening. Reported benefits include the ability to identify and rule out numerous serious abnormalities earlier on, provide reassurance to moms who are at risk earlier on, make genetic diagnoses earlier on, and, if necessary, terminate pregnancies more easily. Some physiological structures and diseases do not manifest until later in life (such as the corpus callosum or a hypoplastic left heart), making early detection difficult and potentially complicating counseling owing to the lack of certainty surrounding the clinical relevance of certain findings; other limitations include the requirement for qualified and experienced personnel and an unclear cost-benefit ratio.[1,3]

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Due to sonography's widespread use in prenatal care, many of these conditions are now identified during pregnancy, leaving both the patient's family and their doctor to consider the option of an elective abortion. In an ideal world, a specific diagnosis would inform the discussion of this subject. Fetal sonography, however, has challenges in making such a diagnosis. Many abortions are carried out based on diagnostic suspicion since, even under ideal circumstances, it is overlooked in at least 35% of cases.[3]

The purpose of this research was to compare 4D-US to 2D-US in the first and second trimesters of pregnancy for the purpose of assessing and detecting fetal congenital abnormalities.

2. Patients and methods

From November 2023 through November 2024, the radiodiagnosis department at Al-Hussein Hospital, Al-Azhar University, conducted a cross-sectional study on 200 pregnant women at high risk during the first and second trimesters. The research was given the green light by the Radiodiagnosis department's ethics board.

Inclusion criteria:

A good family history, many pregnancies, a history of congenital deformity, and a marriage between blood relatives.

Exclusion criteria:

Subjects with normal foetal biometry, women in their third trimester of pregnancy, and those with severe oligohydramnios throughout pregnancy.

Methods:

A variety of ultrasound machines with different types of probes were used throughout the study period(VOLUSON S10&TOSHIBA) with trans-abdominal 5MHz with many degrees of insonation angles and quality.

Women between the ages of 24 and 36 who were evaluated underwent a 4D-anomaly fetus scan after receiving counseling about the potential for aberrant findings. Transvaginal ultrasounds were performed on all first-trimester pregnant women between 13 and 14 weeks into their pregnancies, with the exception of those who came in during the second trimester or who refused to have the procedure done that way. In order to better see the fundal portion of the uterus, they were also inspected trans-abdominally.

Although the sensitivity for significant malformations at 13–14 weeks has been shown to be similar to that of the mid-pregnancy scan, it still can't substitute the mid-pregnancy scan for diagnosing some fetal structural abnormalities, such as heart problems.

Additionally, early scans were unable to detect certain abnormalities, such as hydrocephalus, hydronephrosis, and teratoma, which developed after the first trimester in many of the cases examined.

However, most chromosomal abnormalities in fetuses can be detected as early as the first trimester through increased nuchal translucency and the absence of nasal bone hypoplasia.

We finally reached that the anomaly fetal scan by applications of 4D-sonography has big role in identification and confirmation of many fetal anomalies but has little role in fetal echo sonography and identification of many fetal cardiac anomalies.

Checklist of Fetal Organs at 10–16 Weeks' Screening:

Brain: (cerebellum, form of the skull, plexus chorioideus, lateral ventricles, and midline echo). Check the neck for a normal look and the thickness of the nuchal translucency. To the face: (lensed eyes, nasal bone, a normal profile/mandible, and unbroken lips). The spinal column (the skin on top, as seen in both the longitudinal and transverse views). Coronary artery (angle, four-chamber perspective, symmetry, pulse). The presence, dimensions, form, and relationship to the diaphragm of the stomach... Closure and insertion of the umbilical veins occur on the abdominal wall. Kidneys: (presence, tissue composition, volume, pelvic enlargement). The presence, dimensions, and form of the urinary bladder in humans. Blood: (amount is considered normal if the largest pocket measures 3-8 cm). Bones that extend in all directions: (three-part limbs, normally-oriented hands and feet).

Protocol of fetal scan according to ISUOG: 1

Requirements used for the ultrasound equipment in the First and second trimester scanning:

Two-dimensional ultrasound imaging is done in real time and is available in grayscale. 4D ultrasound transducers, transvaginal in the first trimester, and trans-abdominal at 3.0:5.0 MHz. Standards for output display and controls for adjustable acoustic power output. Zoom in and out, frozen in place. Digital measuring tools with the ability to print and save pictures.

It was crucial to verify viability, precisely determine gestational age, count the foetuses, and evaluate chorionicity and amnionicity in cases of multiple pregnancies for all patients who presented in early pregnancy. The scan allowed for the early detection of noticeable fetal abnormalities towards the end of the first trimester; pregnant women who were suspected of having chromosomal abnormalities or who had a family history of them were screened for aneuploidy and had their nuchal translucency thickness measured (NT).

Preliminary diagnosis was made using the findings after the 2D-sonography was finished. After that, the patients had 3D-US evaluations to see if the 3D-imaging data matched up with the 2D-findings and if the 3D-imaging provided any diagnostic benefits over the 2D-US. In cases where 2D-US indicated an anomaly or recognized a location of interest, a 3D-US volume was acquired to scan the entire body. We also used 4D-US in our protocol, which allowed us to watch the baby's movements in real time. The patient spent around 45 minutes undergoing US for both procedures.

The 3D-US data was kept so that patients could be evaluated and manipulated more after they left the clinic. We showed the pictures as simultaneous topographic views in three planes (transverse, sagittal, and coronal) after rotating the volume sets and setting them up in conventional anatomical orientation.

To distinguish between the characteristics of the bone and soft tissues, images were processed using different filter settings. To capture images of the skeletal framework, the surfacing or transparency mode was employed.

To find out if we got the same, extra, or contradictory information, we compared the 3D-images with the 2D-images, rated and evaluated the results.

When comparing the results acquired with 2D and 3D-US, the 3D-technique was deemed superior in cases where the malformation was spotted or understood more quickly or with better localization, size, and depth, or in cases where a malformation undiscovered with 2D-US was discovered.

Central Nervous System (CNS), Musculoskeletal System (MSK), Gastrointestinal System (GIT), Face and Neck, Miscellaneous, and Genitourinary System (GU) were the eight body systems into which anomalies were categorized. One was not observed, two were slightly visible, and three had outstanding visibility of details when evaluating the clarity of US findings using 2D or 3D/4D technique.

Protocol and technique of heart examination used in all included cases by grey scale and color doppler:

Using a 2D-transducer (3-5 MHz), which is more accurate than a 4D-US evaluation, we were able to rule out the possibility of congenital heart defects in the research fetuses. Lying on their backs, every pregnant woman was present. To confirm the presence of the fetus, a sagittal image was taken; subsequent evaluations were conducted on the baby's right and left sides. Spin the probe around 90 degrees to check the position of the heart, stomach, aorta, and inferior vena cava (IVC).

If you're evaluating a fatal heart, the best place to start is with a cross-section of the thorax to find the four chambers of the heart; this will provide you with the best view of the organ when it is in the same plane as a single rib.

When looking at the aorta from the rear, the left atrium is at the far back. With the right ventricle at the front, we may observe the major vessels by sweeping the probe from the 4-chamber perspective. From the perspective of the four chambers, we can observe the tricuspid valve on the right and the mitral valve on the left, both of which are located slightly away from the heart's apex.

'Moderator band' refers to the layer of smooth muscle that lines the right ventricle. With its apex turned to the left and front, the deadly heart takes up a third of the deadly thorax. The 'foramen oval,' a typical aperture, is situated between the two atria. The tricuspid and mitral valves should be able to move freely and contract when necessary.

Color and pulsed Doppler are used in evaluating the following:

Ductus venosus:

Evaluation, especially at first-trimester scanning, is considered an important evaluation method and helps in early evaluation of congenital heart anomalies and fetal aneuploidies. Originate at the barrel of the junction between right and left portal veins eliasing toward the spine' we used mid sagittal and axial view to fetal abdomen for evaluation, make sure of its normal wave and make sure that the insonation angle is almost parallel to the direction of blood flow in the ductus venosus'S: ventricular systole, D: ventricular diastole and A: atrial contraction'.

Umbilical vessels:

Used color Doppler for evaluating the 3-vessel cord, two arteries, and one vein. Two arteries easily seen by axial view at the fetal pelvis, they are easily seen around the fetal urinary bladder on the mid-sagittal plane, the same plane as the ductus venosus. We can see the umbilical artery and vein. And had a pulsed Doppler waveform of the umbilical artery, a low-resistance waveform with RI less than 0.7.

Statistical analysis:

For the purpose of data entry, an Excel spreadsheet was created. In order to improve accuracy, we implemented validation checks for numerical variables and an option-based data entry mechanism for categorical variables. The statistical packages used for the analyses were SPSS (Statistical Package for the Social Sciences, version 24, SPSS Inc., Chicago, IL, USA). The Shapiro-Wilk Test was used to determine if the data were normally distributed. For numerical data that did not follow a normal distribution, it was expressed as median and inter-quartile range [IQR], or as mean±standard deviation [SD]. Categorical variables were represented using frequency tables that included percentages. Parametric quantitative variables were compared using paired t-tests and independent Student t-tests, while non-parametric quantitative variables were compared using Mann-Whitney tests and the Wilcoxon matched-pairs test. For categorical variables, we utilized chi-square or McNemar-Bowker tests. A p-value is used to calculate statistical significance.

3. Results

Table 1. Demographic characteristics of studied cases.

VARIABLES	DESCRIPTIVE STATISTICS (N=200)
AGE IN YEARS	
MEAN±SD	29.5±5.2
RANGE	21-39
GESTATIONAL AGE IN WEEKS	
MEAN±SD	17.9±4.7
RANGE	10-25
GRAVIDITY	
MEAN±SD	2.56±1.18
MEDIAN(RANGE)	2(1-6)
PARITY	
MEAN±SD	1.18±0.99
MEDIAN (RANGE)	1(0-5)

*Data are presented as mean±SD, median(Range), or number(%)

The mean age of the included women was 29.5±5.2 years, ranged between 21-39 years, the mean gestational age was 17.9±4.7 weeks, ranged between 10-25 weeks, the mean gravidity was 2.56±1.18, ranged between 1-6 times and the mean parity was 1.18±0.99, ranged between 0-5 times,(table 1).

Table 2. Comparison of the spine examination by 2D and 4D compared to pregnancy outcome.

		SPINE ACCORDING TO PREGNANCY OUTCOME		TOTAL	KAPPA AGREEMENT	P-VALUE
		No anomalies	anomalies			
SPINE BY 2D-US	No anomalies	187(95.4%)	4(30.8%)	191(95.5%)	0.808	<0.001*
	Anomalies	0(0%)	9(69.2%)	9(9.5%)		
TOTAL		187(100%)	13(100%)	200(100%)		
SPINE BY 4D-US	No anomalies	187(95.4%)	1(7.7%)	188(94%)	0.957	<0.001*
	Anomalies	0(0%)	12(92.3%)	12(6%)		
TOTAL		187(100%)	13(100%)	200(100%)		

Regarding the comparison of the spine examination by 2D-US and the pregnancy outcome, it was found that, out of 13-cases finally diagnosed with spine anomalies, 9-cases were also diagnosed by 2D-US and the remaining 13-cases were falsely negative for spine anomalies, also all cases who were normal regarding the pregnancy outcome were normal by 2D-US with highly significant percentage of agreement of 0.80.

Regarding the comparison of the spine examination by 4D-US and the pregnancy outcome, it was found that, out of 13-cases finally diagnosed with spine anomalies, 12-cases were also diagnosed by 4D-US and only 1-case was falsely negative for spine anomalies, also all cases who were normal regarding the pregnancy outcome were normal by 4D-US with highly significant percentage of agreement of 0.957,(table 2).

Table 3. Comparison of the head examination by 2D and 4D compared to pregnancy outcome.

		HEAD ACCORDING TO PREGNANCY OUTCOME		TOTAL	KAPPA AGREEMENT	P-VALUE
		No anomalies	anomalies			
HEAD BY 2D-US	No anomalies	180(98.4%)	2(11.8%)	182(91%)	0.84	<0.001*
	Anomalies	3(1.6%)	15(88.2%)	18(9%)		
TOTAL		183(100%)	17(100%)	200(100%)		
HEAD BY 4D-US	No anomalies	180(98.4%)	0(0%)	180(90%)	0.91	<0.001*
	Anomalies	3(1.6%)	17(100%)	20(10%)		
TOTAL		183(100%)	17(100%)	200(100%)		

According to the comparison of the head examination by 2D-US and pregnancy outcome, it was found that, out of 17-cases finally diagnosed with head anomalies, 15-cases were also diagnosed by 2D-US and the remaining 2-cases were falsely negative for head anomalies, also out of 183-cases who were normal regarding the pregnancy outcome, 180-cases were also normal by 2D-US and the remaining 3-cases were falsely positive for head anomalies with highly significant percentage of agreement of 0.84.

According to the comparison of the head examination by 4D-US and pregnancy outcome, it was found that, all the 17-cases finally diagnosed with head anomalies were also diagnosed by 4D-US, also out of 183-cases who were normal regarding the pregnancy outcome, 180-cases were also normal by 4D-US and the remaining 3-cases were falsely positive for head anomalies with highly significant percentage of agreement of 0.91,(table 3).

Table 4. Comparison of the face examination by 2D and 4D compared to pregnancy outcome.

		FACE ACCORDING TO PREGNANCY OUTCOME		TOTAL	KAPPA AGREEMENT	P-VALUE
		No anomalies	Anomalies			
FACE BY 2D-US	No anomalies	185(98.9%)	3(23.1%)	188(94%)	0.78	<0.001*
	Anomalies	2(1.1%)	10(76.9%)	12(6%)		
TOTAL		187(100%)	13(100%)	200(100%)		
FACE BY 4D-US	No anomalies	186(99.5%)	1(7.7%)	187(93.5%)	0.918	<0.001*
	Anomalies	1(0.5%)	12(92.3%)	13(6.5%)		
TOTAL		187(100%)	13(100%)	200(100%)		

According to the comparison of the face examination by 2D-US and pregnancy outcome, it was found that, out of 13-cases finally diagnosed with face anomalies, 10-cases were also diagnosed by 2D-US and the remaining 3-cases were falsely negative for face anomalies, also out of 187-cases who were normal regarding the pregnancy outcome, 185-cases were also normal by 2D-US and the remaining 2-cases were falsely positive for face anomalies with highly significant percentage of agreement of 0.78.

According to the comparison of the face examination by 4D-US and pregnancy outcome, it was found that, out of 13-cases finally diagnosed with face anomalies, 12-cases were also diagnosed by 4D-US and the remaining 1-case was falsely negative for face anomalies, also out of 187-cases who were normal regarding the pregnancy outcome, 186-cases were also normal by 4D-US and the remaining 1-case was falsely positive for face anomalies with highly significant percentage of agreement of 0.918,(table 4).

Table 5. Comparison of the Skeletal examination by 2D and 4D compared to pregnancy outcome.

		SKELETAL ACCORDING TO PREGNANCY OUTCOME		TOTAL	KAPPA AGREEMENT	P-VALUE
		No anomalies	Anomalies			
SKELETAL BY 2D-US	No anomalies	192(99%)	0(0%)	192(96%)	0.85	<0.001*
	Anomalies	2(1%)	6(100%)	8(4%)		
TOTAL		194(100%)	6(100%)	200(100%)		
SKELETAL BY 4D-US	No anomalies	194(100%)	0(0%)	194(97%)	1	<0.001*
	Anomalies	0(0%)	6(100%)	6(3%)		
TOTAL		194(100%)	6(100%)	200(100%)		

According to the comparison of the skeletal examination by 2D-US and pregnancy outcome, it was found that, all of the 6-cases finally diagnosed with skeletal anomalies, they were also diagnosed by 2D-US and out of 194-cases who were normal regarding the pregnancy outcome, 192-cases were also normal by 2D-US and the remaining 2-cases was falsely positive for skeletal anomalies, with highly significant percentage of agreement of 0.85.

According to the comparison of the skeletal examination by 4D-US and pregnancy outcome, it was found that, all cases with skeletal anomalies were correctly identified y 4D-US, also all normal cases were identified correctly by 4D-US with highly significant percentage of agreement of 100%,(table 5).

4. Discussion

The study included 200 high-risk pregnant women, with a mean age of 29.5±5.2 years(ranging between 21-39 years).

Consistent with our findings, Ibrahim et al.,[4] in a study of 100 women, identified consanguinity and increased maternal age as significant risk factors for congenital anomalies.

Regarding obstetric history, the mean gravidity was 2.56±1.18, ranging between 1-6 pregnancies, while the mean parity was 1.18±0.99, with a range of 0-5 live births.

Supporting these findings, Zhang et al.,[5] found that the birth defect group had significantly higher gravidity, parity, preterm birth rate, cesarean section(CS) rate, scarred uterus, stillbirths, and male newborns compared to the control group, reinforcing the impact of obstetric history on fetal outcomes.

The early and accurate diagnosis of CNS anomalies(head and spine) is crucial for guiding clinical decisions and parental counseling. In this study, we compared the detection rates of CNS anomalies using 2D-US, 4D-US, and actual pregnancy outcomes to evaluate the diagnostic accuracy of both modalities. Our findings revealed that spinal anomalies were detected in 4.5% of cases by 2D-US, 6% by 4D-US, and 6.5% based on pregnancy outcome, while head anomalies were identified in 9% of cases by 2D-US, 10% by 4D-US, and 8.5% based on pregnancy outcome. Both 2D and 4D-US accurately diagnosed major CNS anomalies such as Holoprosencephaly, Anencephaly, Encephalocele, and Spinal mass. However, 4DUS demonstrated superior accuracy in identifying more intricate CNS anomalies, correctly diagnosing Cervical meningocele, Hydrocephalus, and Mega cisterna magna.

These results suggest that 4D-US has a higher detection rate for spinal anomalies compared to 2D-US, aligning more closely with actual pregnancy outcomes. This could be attributed to the enhanced spatial resolution and volumetric imaging capabilities of 4D-US, which allow for better visualization of fetal structures, particularly in complex cases.

Our findings are consistent with previous studies demonstrating the added value of 4D-US in fetal neuroimaging. El-Hameed et al.,[6] compared 4D and 2D ultrasound for detecting CNS anomalies and found that 4D-US correctly diagnosed 71.4% of spinal anomalies, significantly higher than 14.3% with 2D-US(P=0.03). Additionally, 4D-US correctly identified 64.7% of head anomalies, compared to only 23.5% with 2D-US(P=0.015). 2D-US had a high rate of indefinite diagnoses(85.7% for spine anomalies and 76.5% for head anomalies), indicating greater difficulty in clearly identifying these anomalies. These findings confirm that 4D-ultrasound provides superior visualization of fetal CNS structures, reducing diagnostic uncertainty and improving prenatal counseling and decision-making.

Accurate prenatal detection of facial anomalies is essential for early intervention and parental counseling. This study compared the diagnostic accuracy of 2D ultrasound and 4D US in identifying facial anomalies, using pregnancy outcomes as the reference standard. Our findings revealed that facial anomalies were detected in 6% of cases by 2D-US, 6.5% by 4D-US, and 6.5% based on pregnancy outcomes, suggesting a slightly higher detection rate with 4D-US.

These findings emphasize the advantages of 4D-US in visualizing complex facial structures, as its real-time volumetric imaging provides a more detailed assessment of anomalies such as cleft lip, palate, and micrognathia. Previous studies have also highlighted the superior diagnostic accuracy of 4D-US for facial abnormalities, particularly in cleft lip and micrognathia, where 2D-US may have limitations due to its planar imaging approach.

Accurate prenatal detection of skeletal and extremity anomalies is crucial for early diagnosis, parental counseling, and perinatal management. This study compared the diagnostic accuracy of 2D and 4D-US in detecting upper limb, lower limb, and skeletal anomalies, using pregnancy outcomes as the reference standard.

For skeletal anomalies, 2D-US detected a slightly higher number of cases(4%) compared to 4D-US(3%), while pregnancy outcomes confirmed 3%. Both modalities successfully identified all cases of osteogenesis imperfecta, demonstrating strong diagnostic agreement for this severe skeletal disorder. Renal agenesis was correctly diagnosed by 4D-US, further demonstrating its ability to detect structural abnormalities affecting multiple systems. However, 2D-US diagnosed two cases of scoliosis with hemivertebrae, which were not confirmed by either 4D-US or pregnancy outcomes, suggesting a higher false-positive rate with 2D-US. This discrepancy may be attributed to the planar nature of 2D-imaging, which can lead to misinterpretation of fetal spinal curvature, whereas 4D-US provides a more realistic volumetric assessment.

Our findings align with Samadony et al.,[7] and Yousef et al.,[8] who reported that 4D-US significantly improved diagnostic confidence in detecting skeletal and limb anomalies compared to 2D-US. Prenatal detection of spinal anomalies is essential for early diagnosis, parental counseling, and perinatal management. Our study compared the diagnostic accuracy of 2D and 4D-US in detecting spinal anomalies, using pregnancy outcomes as the reference standard. The findings highlight the superior performance of 4D-US over 2D-US in accurately identifying spinal abnormalities.

In our study, 2D-US correctly diagnosed 9 out of 13 confirmed cases of spinal anomalies, while the remaining 4 cases were false negatives, leading to a significant percentage of agreement of 0.80 with pregnancy outcomes. Additionally, all normal cases according to pregnancy outcomes were also reported as normal by 2D-US, indicating that while 2D-US is reliable in confirming normal spinal anatomy, it has limitations in detecting certain anomalies.

Conversely, 4D-US demonstrated superior diagnostic accuracy, correctly identifying 12 out of 13 confirmed spinal anomalies, with only one false-negative case. The agreement between 4D-US and pregnancy outcomes was significantly higher(0.957) compared to 2D-US(0.80), reinforcing the greater sensitivity of 4D-US in visualizing spinal defects. The volumetric imaging capabilities of 4D-US allow for better assessment of spinal curvature, segmentation, and structural integrity, which may explain its enhanced diagnostic performance.

These findings are consistent with previous studies, including Wataganara et al.,[9] which reported that 4D-US was advantageous in detecting 60.8% of fetal anomalies compared to 2D-US.

4. Conclusion

The findings underscore the added diagnostic value of 4D-US in prenatal screening, particularly in high-risk pregnancies. While 2D-US remains the primary screening modality, the superior sensitivity and specificity of 4D-US support its role as an adjunctive imaging tool, enhancing early detection and improving perinatal outcomes.

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