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Review Article

Non-invasive assessment of fetal lung maturity: the role of pulmonary artery Doppler and AT/ET ratio in predicting respiratory distress syndrome

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ABSTRACT

Respiratory distress syndrome (RDS) remains a primary cause of neonatal morbidity and mortality. Traditional fetal lung maturity (FLM) assessment relies on invasive amniocentesis, which carries inherent risks. Fetal pulmonary artery Doppler, specifically evaluating the acceleration time to ejection time (AT/ET) ratio and peak systolic velocity (PSV), has emerged as a reliable non-invasive alternative to evaluate downstream pulmonary vascular resistance. A narrative review of current, peer-reviewed literature was conducted to evaluate the physiological basis, standardized ultrasonographic technique, and clinical applicability of the AT/ET ratio in predicting neonatal RDS, incorporating real-world clinical caveats. As fetal lungs mature, pulmonary vascular resistance decreases, significantly prolonging the pulmonary artery acceleration time and increasing the AT/ET ratio. Clinical evidence demonstrates that an AT/ET cut-off value near 0.30-0.31 provides optimal diagnostic accuracy in normally grown fetuses. However, values directly on the 0.30 threshold constitute a "gray zone" requiring integration with other biophysical markers, such as the PSV. Furthermore, conditions such as gestational diabetes mellitus and fetal growth restriction (FGR) independently alter these indices; notably, chronic hypoxia in FGR mandates significantly lower population-specific thresholds (e.g., AT/ET <0.19) to accurately predict neonatal respiratory complications. The fetal pulmonary artery AT/ET ratio is a highly reproducible and accessible bedside tool for assessing FLM. Integrating this parameter into routine obstetric ultrasound optimizes perinatal outcomes, safely guides the administration of antenatal corticosteroids, and reduces reliance on invasive diagnostic procedures, provided it is interpreted as an adjunct to primary maternal indications for delivery.

Keywords: Fetal organ maturity, Pulmonary artery, Doppler ultrasonography, Respiratory distress syndrome, AT/ET ratio, Gestational diabetes, Fetal growth restriction

INTRODUCTION

Respiratory distress syndrome (RDS) secondary to fetal lung immaturity remains the leading cause of early neonatal morbidity and mortality, placing a profound burden on neonatal intensive care units globally. Beyond acute respiratory failure, RDS is intrinsically linked to severe long-term complications, including bronchopulmonary dysplasia and adverse neurodevelopmental outcomes.[1] Historically, the evaluation of fetal lung maturity (FLM) relied heavily on the analysis of amniotic fluid obtained via amniocentesis. Although recent meta-analyses demonstrate that amniocentesis is generally a safe procedure with very low complication rates even in the setting of threatened preterm labor, it remains an invasive technique that

requires specific maternal-fetal expertise, generates patient anxiety, and carries a non-zero risk of transient complications such as iatrogenic membrane rupture or bleeding.[2] Furthermore, the laboratory turnaround time for biochemical tests often limits their utility in acute triage settings.

Consequently, modern maternal-fetal medicine has shifted towards the development of non-invasive, ultrasound-based diagnostic modalities. Specifically, the evaluation of the fetal main pulmonary artery (MPA) waveforms reflects the physiological decline in pulmonary vascular resistance (PVR) that accompanies lung maturation. As fetal lungs mature and PVR decreases, the right ventricular afterload drops, leading to a measurable increase in the Peak Systolic Velocity (PSV) and a prolongation of the pulmonary artery acceleration time (PAAT). The initial landmark study by Azpurua et al established that this physiological transition is most accurately captured by an increased acceleration time to ejection time (AT/ET) ratio.[3]

Recent prospective studies have further validated that an abnormally low AT/ET ratio, alongside a blunted PSV, are strongly and independently associated with an increased risk of RDS. Current data demonstrates that the diagnostic performance of these specific fetal MPA Doppler indices is highly accurate, providing obstetricians with a reliable, real-time framework for critical decision-making without the risks of invasive testing.[4]

This narrative review aims to synthesize the current, peer-reviewed evidence regarding the physiological basis, ultrasonographic technique, and real-world clinical applicability of the AT/ET ratio in predicting neonatal RDS, providing obstetricians with a practical framework for critical decision-making.

PHYSIOLOGICAL BASIS: HEMODYNAMICS AND LUNG DEVELOPMENT

Dynamics of pulmonary vascular resistance (PVR)

Throughout most of the pregnancy, the fetal lungs are fluid-filled and participate minimally in gas exchange. This low-flow state is actively maintained by a high PVR, mediated by mechanical compression from fluid-filled alveoli and physiological hypoxic pulmonary vasoconstriction. As gestation progresses towards term, the maturation of the pulmonary vascular bed (characterized by the progressive thinning of the arteriolar smooth muscle layer) leads to a gradual but steady decline in PVR, an essential prerequisite for the dramatic increase in pulmonary perfusion required at birth.

Ultrasonographic translation of hemodynamics

The fetal right ventricle (RV) pumps blood directly against this pulmonary vascular bed; therefore, right ventricular afterload is highly dependent on PVR. The Doppler flow velocity waveform of the main pulmonary artery acts as a real-time, non-invasive barometer of this downstream resistance.

In early to mid-gestation, the high PVR creates a strong and early reflection of the systolic pulse wave, effectively shortening the PAAT and occasionally creating a characteristic "spike and dome" morphologic pattern. Conversely, as the fetal lungs mature and PVR drops in the third trimester, the downstream vascular bed becomes more compliant. The systolic wave reflection is delayed, which broadens the Doppler waveform, prolonging the PAAT and increasing the AT/ET ratio.[3,4] Thus, the AT/ET ratio serves as a precise hemodynamic proxy for the maturation of the fetal lung.

METHODOLOGY AND ULTRASOUND EVALUATION TECHNIQUE

Image acquisition and anatomical planes

Accurate measurement of the fetal pulmonary artery Doppler indices requires adherence to standardized echocardiographic planes during a period of fetal quiescence. The primary anatomical window is the right ventricular outflow tract (RVOT) or the three-vessel and trachea (3VT) view. The main pulmonary artery (MPA) is identified as it exits the right ventricle, and the pulmonary valve must be clearly visualized (Figure 1).[3,5]

Doppler optimization and real-world caveats

The pulsed-wave (PW) Doppler gate (sample volume) should be adjusted to 2-3 mm and placed precisely distal to the pulmonary valve leaflets. While minimizing the angle of insonation (<20 degrees) is standard practice for evaluating true velocities (such as PSV), it is crucial to note that time intervals (AT and ET) are mathematically independent of the Doppler angle. Therefore, in real-world scenarios-such as advanced gestation, maternal obesity, or oligohydramnios-clinicians should prioritize obtaining a crisp, well-defined waveform envelope over perfect angular alignment.[4] Angle correction software should not be used, and the sweep speed should be maximized (e.g., up to 15 cm/s) to stretch the waveforms horizontally, allowing for precise temporal caliper placement.

Waveform analysis and Caliper placement

Measurements are ideally obtained and averaged from three to five uniform, consecutive cardiac cycles:[3]

PAAT: Measured from the onset of the systolic waveform to the point of peak systolic velocity.

ET: Measured from the onset of the systolic waveform to the end of the systolic flow (return to baseline).

The AT/ET ratio is calculated by dividing the PAAT by the ET, effectively normalizing the acceleration time

against the total duration of right ventricular systole. (Figure 2).

CLINICAL EVIDENCE AND REFERENCE VALUES

Correlation with gestational age and reference nomograms

The fetal pulmonary circulation undergoes continuous dynamic changes throughout pregnancy. Consequently, normal reference ranges for the AT/ET ratio are highly dependent on gestational age. Nomograms developed in recent large cohort studies demonstrate a positive correlation between the AT/ET ratio and advancing gestation. For instance, recent reference ranges established by Jantarasaengaram et al and Phuakpoolpol et al provide percentile calculators for spectral Doppler parameters from 18 to 40 weeks of gestation.[5,6] These studies confirm that the pulmonary acceleration time significantly increases as the fetus approaches term, directly mirroring the histological canalicular-to-saccular transition and the progressive drop in pulmonary vascular resistance (Figure 3).

Diagnostic performance and cut-off values

Recent prospective clinical research has focused on determining the optimal AT/ET threshold to predict neonatal RDS. In a 2023 study by Hassan et al., researchers demonstrated a statistically significant decrease in the AT/ET ratio among fetuses that subsequently developed RDS compared to those with mature lungs.[4] Based on current evidence, the following clinical thresholds are widely recognized:

Values ≥0.31: Strongly correlate with a mature fetal lung profile, suggesting a minimal risk of severe RDS.

Values <0.30: Are significantly associated with an immature lung profile and a high risk of requiring exogenous surfactant.

The clinical "gray zone" (exactly 0.30): It is crucial to acknowledge that an AT/ET ratio of exactly 0.30 represents a borderline threshold. In such cases, the Doppler indices must not be interpreted in isolation. Obstetricians should integrate this finding with other biophysical parameters to avoid premature interventions.

Crucially, direct comparative studies have historically validated these sonographic findings against invasive gold standards. Foundational research comparing fetal pulmonary artery Doppler indices directly with amniotic fluid biochemical tests (e.g., the surfactant/albumin ratio) demonstrated a strong correlation, establishing that the AT/ET ratio provides comparable diagnostic accuracy for RDS prediction without the inherent risks of amniocentesis.[7]

Confounding factors: gestational diabetes mellitus and fetal growth restriction

When applying standard cut-off values, clinicians must account for underlying maternal conditions that alter fetal hemodynamics and physiological maturation. In pregnancies complicated by gestational diabetes mellitus (GDM), the hyperinsulinemic state is known to delay fetal lung maturation. Recent studies specifically evaluate the AT/ET ratio in this high-risk population. Wang et al demonstrated that the AT/ET ratio can reliably predict neonatal respiratory disorders in women with GDM, providing critical assistance in clinical management.[8] Furthermore, a 2025 prospective study by Ezveci et al confirmed the high predictability of fetal pulmonary artery Doppler on neonatal outcomes in GDM, emphasizing that these non-invasive indices remain a robust diagnostic tool even when maternal metabolic conditions alter standard physiological timelines.[9]

Similarly, in fetuses with fetal growth restriction (FGR) or small for gestational age (SGA), the chronic hypoxic environment increases placental and pulmonary vascular resistance. A 2025 prospective cohort study by Bulan et al. demonstrated that FGR fetuses exhibit significantly higher main pulmonary artery pulsatility indices and lower AT/ET ratios compared to appropriately grown controls. Furthermore, an abnormally low AT/ET ratio (<0.19) in this high-risk population emerged as a powerful, independent predictor of composite adverse pulmonary outcomes, including the need for mechanical ventilation and intensive care admission.[10] These findings highlight how altered intrauterine growth independently modifies right ventricular afterload, necessitating population-specific sonographic cut-offs. (Table 1).

Table 1: Summary of clinical scenarios and the prognostic utility of the fetal pulmonary artery AT/ET ratio.

Clinical scenario	Relevant studies	At/et key finding/ cut-off	Clinical implication
Uncomplicated pregnancies	Azpurua (2010), Hassan (2023)	< 0.30-0.31	High risk of neonatal respiratory distress syndrome (RDS).
PPROM	Duncan (2020)	< 0.305	Predicts RDS, but must be integrated with gestational age.

Continued.

Clinical scenario	Relevant studies	At/et key finding/ cut-off	Clinical implication
Gestational diabetes mellitus (GDM)	Wang (2022), Ezveci (2025)	Lower values for equivalent gestational age.	Reflects delayed lung maturation due to fetal hyperinsulinemia.
Antenatal corticosteroid therapy	Vafaei (2021)	Significant ratio increases within 24-48 hours.	Serves as a real-time biophysical marker of therapeutic response.
Fetal growth restriction (FGR/SGA)	Bulan (2025)	<0.19	Severe chronic hypoxia mandates a much lower threshold to predict RDS and mechanical ventilation.

AT/ET: Acceleration time to ejection time ratio; RDS: Respiratory Distress Syndrome.

Table 2: Dynamic changes in fetal pulmonary artery AT/ET ratio following antenatal betamethasone (ACS) administration.

Clinical group / time interval	AT/ET ratio (mean±SD)	Physiological significance
Control group (baseline / non-exposed)	0.214±0.031	Baseline pulmonary vascular resistance for early preterm gestation (26–34 weeks).
Exposed group (24 to 48 hours post-ACS)	0.229±0.043*	Significant reduction in resistance mirroring active surfactant synthesis.

ACS: Antenatal corticosteroids; AT/ET: Acceleration time to ejection time ratio; SD: Standard Deviation;*p < 0.05 indicates a statistically significant increase compared to the non-exposed baseline group. Data adapted from Vafaei et al.[12]

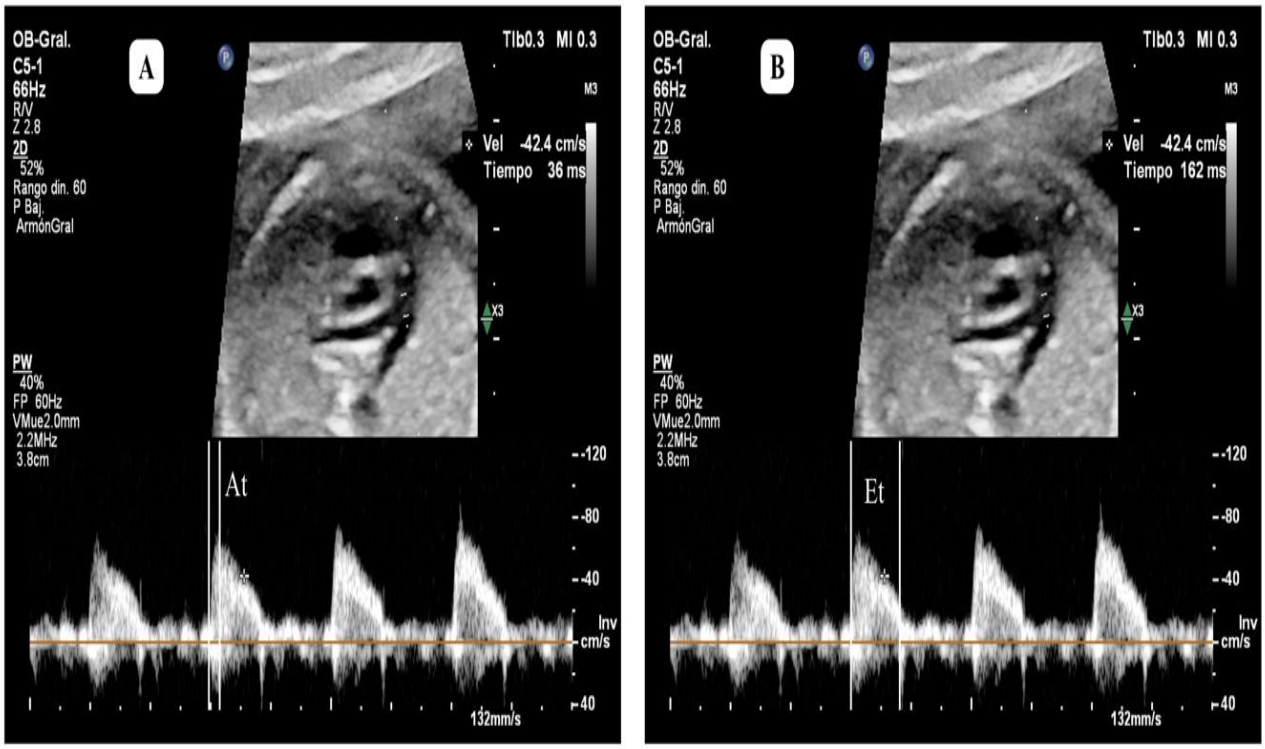

Figure 1: Spectral Doppler waveform analysis of the fetal main pulmonary artery; (A) measurement of the acceleration time (AT). Calipers are placed from the onset of the systolic flow to the point of peak systolic velocity (recorded as 36 ms). (B) Measurement of the Ejection Time (ET). Calipers are placed from the onset of the systolic flow to the end of the forward ventricular ejection, where the waveform returns to the baseline (recorded as 162 ms). Note the use of a high sweep speed (132 mm/s) to stretch the waveform horizontally, allowing for highly precise temporal caliper placement. For this specific cardiac cycle, the calculated AT/ET ratio is 0.22

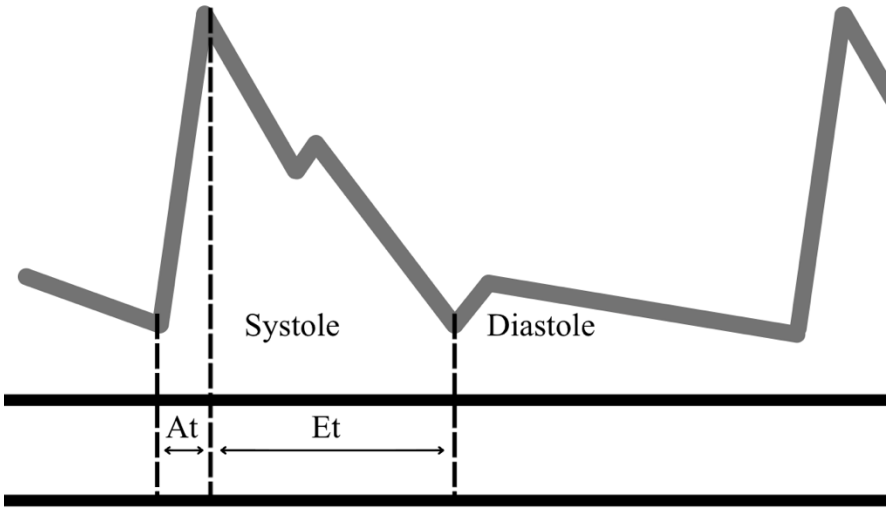

Figure 2: Schematic diagram illustrating precise caliper placement. AT is measured from start of systolic flow to peak velocity. ET is measured from start to end of systolic flow, where the waveform returns to the baseline.

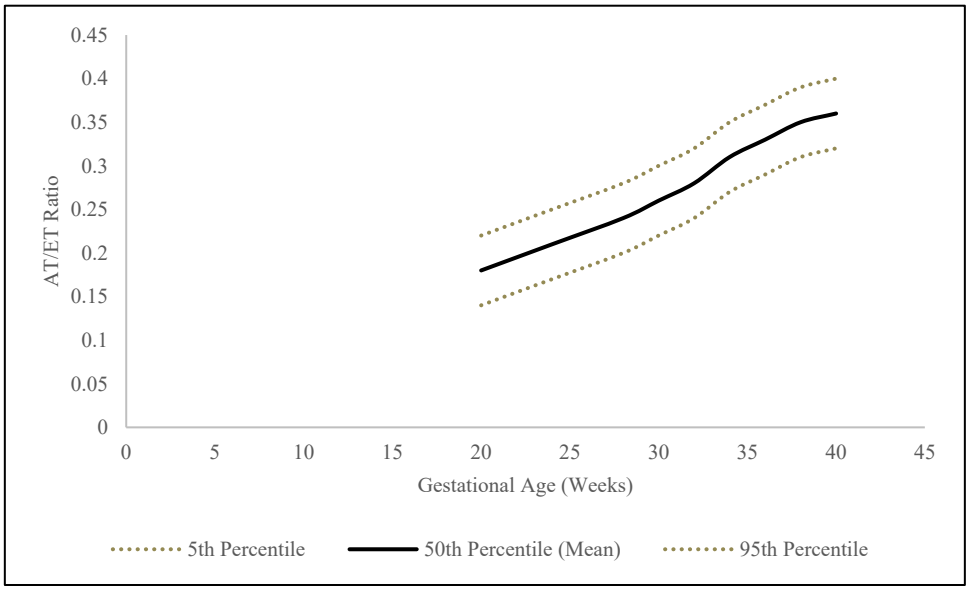

Figure 3: Progression of the fetal pulmonary artery AT/ET ratio across advancing gestational age, reflecting the physiological decline in downstream pulmonary vascular resistance during the canalicular and saccular stages of lung development.

CLINICAL APPLICATION IN OBSTETRICS

Triage in preterm premature rupture of membranes (PPROM)

In the acute setting of PPROM, the AT/ET ratio obtained at the bedside provides immediate prognostic information. However, its interpretation requires clinical nuance. A study by Duncan et al evaluating the AT/ET ratio in PPROM pregnancies demonstrated its utility in predicting RDS; nonetheless, their findings also underscored that gestational age at delivery remained an independent and highly powerful predictor.[11] Thus, the Doppler indices should complement, rather than replace, clinical algorithms based on gestational age in PPROM triage.

Guiding antenatal corticosteroid therapy

The administration of antenatal corticosteroids (ACS) is a cornerstone of preterm labor management. Interestingly,

the AT/ET ratio can also reflect the therapeutic effect of these drugs. Recent evaluations by Vafaei et al demonstrate that betamethasone administration in pregnancies at risk for preterm birth leads to significant alterations in fetal pulmonary artery Doppler indices, reflecting drug-induced acceleration of lung maturation and changes in pulmonary hemodynamics. Their findings confirm that these hemodynamic shifts, characterized by a measurable and statistically significant increase in the AT/ET ratio, occur within 24 to 48 hours following the first dose of betamethasone, precisely mirroring the physiological window of accelerated surfactant release.[12] This dynamic response further validates the AT/ET ratio as a functional, real-time marker of lung maturity (Table 2).

Timing of delivery in high-risk pregnancies

Maternal Priority By objectively quantifying the degree of lung maturity, the AT/ET ratio empowers the clinician to optimally time the delivery when feasible. Nevertheless, it is paramount to emphasize that the AT/ET ratio should never override primary maternal indications for delivery. In conditions such as severe early-onset preeclampsia with impending maternal decompensation, the immediate resolution of pregnancy remains the absolute priority regardless of the fetal pulmonary Doppler indices. In these critical scenarios, the AT/ET ratio serves merely as an adjunct to anticipate the level of neonatal respiratory support required upon birth, rather than a criterion to delay delivery.

LIMITATIONS AND FUTURE PERSPECTIVES

While the clinical utility of the AT/ET ratio is supported by solid evidence, critical limitations exist. First, the acquisition of high-quality Doppler waveforms requires moderate sonographic expertise, and unfavorable fetal lie can compromise image quality. However, studies assessing the reproducibility of fetal pulmonary artery velocimetry demonstrate acceptable inter-observer and intra-observer variability with low coefficients of variation, indicating that the learning curve for this technique is highly manageable with standardized training.[3]

Another physiological limitation is the influence of the fetal heart rate (FHR). Because the ejection time (ET) is inversely proportional to the heart rate, significant fetal tachycardia or bradycardia can artifactually alter the AT/ET ratio.[13] Although the ratio itself partially corrects for these variations compared to measuring PAAT alone, clinicians must interpret the indices cautiously in the presence of fetal arrhythmias or severe FHR baseline deviations. Future research should focus on whether management protocols guided exclusively by the AT/ET ratio yield superior perinatal outcomes compared to standard clinical care in large, multicenter randomized trials.

Furthermore, a notable gap in the current literature is the absence of validated AT/ET nomograms for multiple gestations, where hemodynamic adaptations and lung maturation timelines may differ significantly from singletons.

Looking forward, it is imperative to contextualize the AT/ET ratio against other emerging non-invasive technologies, particularly artificial intelligence (AI) and quantitative ultrasound texture analysis (such as QuantusFLM). Recent comparative evaluations by Abdelhamid et al indicate that while AI-driven texture analysis offers high diagnostic accuracy for predicting RDS, the fetal pulmonary artery AT/ET ratio demonstrates a highly comparable predictive value.[14] Furthermore, studies such as those by Zamarian et al validate that these AI-driven texture analyses maintain their high predictive accuracy even in high-risk groups like fetal growth restriction.[15] However, the distinct advantage of the Doppler assessment lies in its real-time, bedside applicability; it does not require off-line post-processing, internet connectivity, or proprietary external software, making it highly accessible in acute obstetric triage. Future research should focus on combined predictive models integrating both Doppler hemodynamics and AI-driven texture analysis to maximize diagnostic precision and definitively replace invasive testing.

CONCLUSION

The non-invasive assessment of fetal lung maturity using the pulmonary artery acceleration time (PAAT) and the AT/ET ratio represents a significant, evidence-based advancement in maternal-fetal medicine. By reflecting the physiological decline in pulmonary vascular resistance, the AT/ET ratio provides an accurate bedside tool to predict the risk of neonatal RDS. Integrating this parameter into routine obstetric triage empowers clinicians to make informed decisions regarding the timing of delivery and targeted corticosteroid administration. However, it is essential that these indices are interpreted within the broader clinical context, accounting for conditions that alter baseline fetal hemodynamics-such as fetal growth restriction or gestational diabetes-which may necessitate population-specific diagnostic thresholds. Ultimately, these sonographic tools must serve as an adjunct to, rather than a replacement for, clinical judgment, always prioritizing maternal stability in high-risk obstetric scenarios.

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