Serial lung mass volume ratios as prognostic indicators of neonatal respiratory morbidity in fetal pulmonary malformations

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BACKGROUND: Several studies have shown that the congenital pulmonary airway malformation volume ratio is a useful prognosticator of neonatal outcome in prenatally diagnosed lung lesions. However, there remains a lack of consensus on which congenital pulmonary airway malformation volume ratio values have the best predictive value because of operator dependence, inherent changes in lung lesion size throughout gestation, and the widespread use of maternal steroids.

OBJECTIVE: This study sought to determine the association between serial congenital pulmonary airway malformation volume ratio measurements and neonatal outcomes among fetuses with lung malformations.

STUDY DESIGN: This was a retrospective cohort study of fetuses with a prenatally diagnosed lung malformation managed at 2 major fetal centers from January 2010 to December 2021. Prenatal variables, including prospectively measured congenital pulmonary airway malformation volume ratio measurements (initial, maximum, and final), were analyzed. The results were correlated with 3 outcome measures, namely surgical resection before 30 days of life, a need for supplemental O_2 at birth, and endotracheal intubation at birth. Statistical analyses were performed using receiver operating characteristic curve analyses, Welch 2 sample *t* tests, and multivariable logistic regressions ($P<.05$).

RESULTS: There were 123 fetuses with isolated lung lesions identified. Eight (6.5%) had hydrops. The mean initial congenital pulmonary airway malformation volume ratio was 0.67±0.61 cm^2 at 22.9±3.9 weeks' gestation. The mean maximum congenital pulmonary airway malformation volume ratio was 1.08 ± 0.94 cm^2 at 27.0 ± 4.0 weeks' gestation. The mean final congenital pulmonary airway malformation volume ratio was 0.58±0.60 cm^2 at 33.2±4.1 weeks' gestation. At a mean gestational age at delivery of 38.3±2.6 weeks, 15 (12.2%) underwent neonatal lung resection for symptomatic disease. In a multivariable regression, all 3 congenital pulmonary airway malformation volume ratio measurements showed a significant correlation with neonatal lung resection ($P<.001$). Optimal congenital pulmonary airway malformation volume ratio cutoffs were established based on an initial congenital pulmonary airway malformation volume ratio of ≥0.8 cm^2, maximum congenital pulmonary airway malformation volume ratio of ≥1.5 cm^2, and a final congenital pulmonary airway malformation volume ratio of ≥1.3 cm^2 with associated areas under the curve of 0.89, 0.97, and 0.93, respectively. The final congenital pulmonary airway malformation volume ratio had the highest specificity for predicting surgical lung resection in the early postnatal period.

CONCLUSION: Measuring congenital pulmonary airway malformation volume ratios throughout pregnancy in fetuses with pulmonary malformations has clinical value for prenatal counseling and planning care transition after delivery. Fetuses with a final congenital pulmonary airway malformation volume ratio of more than 1.3 cm^2 are likely to require neonatal surgery and therefore should be delivered at tertiary care centers with a neonatal intensive care unit and pediatric surgical expertise.

Key words: bronchopulmonary sequestration, congenital pulmonary airway malformation, CVR, fetal ultrasound, hydrops, maternal steroids, neonatal surgery, prenatal counseling, prenatal diagnosis

Introduction

Congenital lung malformations (CLMs) represent a group of heterogenous pathologies that include congenital pulmonary airway malformations (CPAM) (formerly called cystic adenomatoid malformation), bronchopulmonary sequestrations (BPS), bronchogenic cysts, and congenital lobar emphysemas.[1,2] Although rare, antenatal recognition has increased over the past several decades, occurring in approximately 1 in 2500 live births.[3] The majority of CLMs are diagnosed before birth in accordance with the widespread use of obstetrical sonography and advances in ultrasonography sensitivity and resolution.[4]

There is a wide range of postnatal outcomes for fetuses with CLMs.[4,5] Approximately 80% of fetuses will be completely asymptomatic at birth and do not have any pulmonary morbidity in early infancy, whereas the remaining 20% will incur an array of prenatal and/or postnatal complications, including hydrops, in utero demise, and respiratory compromise secondary to mass effect with or without air trapping.[6–8] Lesion size, and not histology, has been found to hold the most prognostic value.[9]

The CPAM volume ratio (CVR), an ultrasonographic measurement of CLM size relative to head circumference, was originally described as a sonographic measurement tool for assessing the risk for fetal hydrops and the need for prenatal surgery among those with cystic adenomatoid lesions.[10] Subsequent studies have demonstrated that the CVR can be a useful parameter to inform delivery planning because of its significant correlation with respiratory distress and neonatal surgery.[7,11,12] Despite these data, a recent systematic review suggested that there remains a lack of consensus on the use of CVR measurements for predicting postnatal morbidity and the need for delivery at a specialized center.[13] Serial CVR measurements often show a doubling in size

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AJOG MFM at a Glance

Why was this study conducted?

Fetuses with a congenital lung malformation have a wide spectrum of potential clinical outcomes, ranging from in utero demise to asymptomatic disease. Less than 20% of those fetuses will have respiratory symptoms at birth and will require neonatal lung resection. Several studies have suggested that the congenital pulmonary airway malformation volume ratio (CVR) is a useful sonographic measurement for identifying newborns with increased respiratory morbidity. However, little is known about the relationship between different CVRs obtained throughout pregnancy and early postnatal outcomes.

Key findings

The CVR among fetuses with a lung malformation is highly variable depending on gestational age. Although an increased initial, maximum, and final CVR were each associated with an increased risk for requiring a neonatal lung resection, a final CVR $\geq$1.3 cm^2, measured at a mean of 33 weeks' gestation, had the highest specificity for predicting surgical disease in the early postnatal period.

What does this add to what is known?

Measuring CVRs throughout pregnancy for fetuses with pulmonary malformations has clinical value for prenatal counseling and for planning delivery and neonatal care transition. Fetuses with a final CVR >1.3 cm^2 are substantially more likely to require neonatal surgery and therefore should be delivered at tertiary care centers with a neonatal intensive care unit and pediatric surgical expertise.

by 25 to 27 weeks' gestation before leveling off or spontaneously regressing during the third trimester.[14–18] The initial CVR at the time of referral (initial CVR), the maximum CVR during gestation (maximum CVR), and the final CVR measured closer to term (final CVR) have all been touted as helpful predictors of neonatal outcome,[7,12,19–21] but there have only been a few comparative studies focused on the relative diagnostic accuracy of CVR measurements obtained serially throughout gestations.

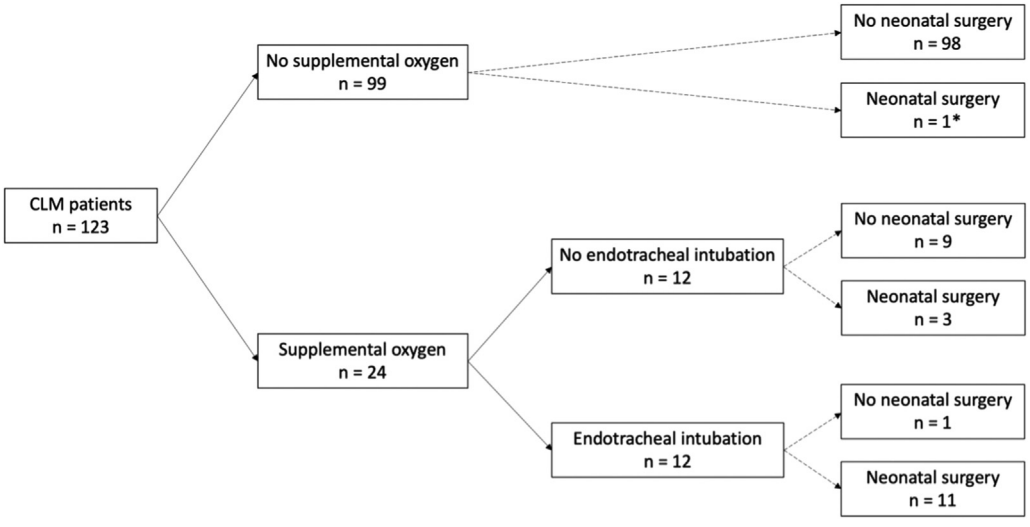
In this study, we used a multicenter fetal registry to determine the association between serial CVR measurements and neonatal outcome among fetuses with CLMs. Our group hypothesized that although initial, maximum, and final CVR measurements are significantly associated with postnatal outcome, the final CVR would have the highest diagnostic accuracy for predicting neonatal resection, regardless of other prenatal factors.

Materials and Methods

Study design and population

This study was approved by the institutional review boards at 2 separate institutions (IRB00296598, IRB00207285). The manuscript followed the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for observational studies. A retrospective chart review was conducted of liveborn

FIGURE 1
Postnatal course of 123 fetuses with an isolated lung malformation



An *asterisk* denotes persistent tachypnea noted at birth.

CLM, congenital lung malformations.

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TABLE 1
Association of CVR measurements and neonatal outcome in fetal lung malformations

A. Neonatal resection

Variable	Yes (n=24)	No (n=99)	*P*
Initial CVR	1.64 (0.97)	0.54 (0.40)	<.001
Maximum CVR	2.91 (1.20)	0.86 (0.61)	<.001
Final CVR	1.77 (0.87)	0.42 (0.32)	<.001

B. Supplemental O_2

Variable	Yes (n=12)	No (n=111)	*P*
Initial CVR	1.23 (0.97)	0.53 (0.38)	.003
Maximum CVR	1.99 (1.48)	0.88 (0.62)	.002
Final CVR	1.20 (1.00)	0.43 (0.32)	.001

C. Endotracheal intubation

Variable	Yes (n=15)	No (n=108)	*P*
Initial CVR	1.89 (0.95)	0.54 (0.39)	<.001
Maximum CVR	2.88 (1.40)	0.9 (0.66)	<.001
Final CVR	1.81 (0.90)	0.44 (0.35)	<.001

All CVR values are expressed as the mean (standard deviation).

CVR, congenital pulmonary airway malformation volume ratio.

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patients with a CLM who were included in prospectively managed databases maintained at site A (January 1, 2010 to December 31, 2021) and site B (January 1, 2010 to December 31, 2018). For CLM referrals, both sites were integrated referral centers that (1) routinely calculated the CVR at each ultrasound evaluation, (2) had the full spectrum of fetal intervention capabilities, and (3) offered on-site obstetrical and pediatric care. For a subset of these patients at site B (n=38), detailed sonographic data on lung malformations in relation to respiratory morbidity have been reported previously as part of a multicenter study.[17]

Data collection

All fetuses underwent serial 2D sonograms (Phillips IU-22, Andover, MA; General Electric Voluson 730 (E10), Waukesha, WI) performed by a board-certified maternal-fetal medicine specialist. Prenatal characteristics, such as the presence of hydrops, CVRs with associated gestational age, and any fetal intervention, were collected. The 3-dimensional size of an echogenic lesion was prospectively measured (in cm) to calculate a CVR.[10] Briefly, the CVR was obtained by taking the product of the length, width, and depth of the mass, multiplying by a 0.523 correction factor (assuming its shape as a prolate ellipse), and then dividing by the head circumference to normalize for gestational age. The initial CVR at referral, maximum CVR, and final CVR recorded before delivery were documented.

Fetal hydrops was defined as the presence of fluid in 2 or more spaces, including ascites, pleural effusion, pericardial effusion, or subcutaneous edema, usually with supporting echocardiographic evidence of cardiac dysfunction.[22] Maternal steroids were given at the discretion of the managing maternal-fetal medicine specialist based on CVR size, growth trends, and microcystic characteristics.[23] The primary outcome measure was neonatal surgery, defined as lung resection performed within 30 days of life because of the presence of symptomatic respiratory disease. Secondary outcome measures were documented preoperative supplemental O_2 and endotracheal intubation.

Statistical analysis

All values were reported as the mean and standard deviation unless otherwise indicated. Statistical analyses, including Welch 2 sample *t* tests and multivariable logistic regression, were performed using R studio software (version 2022.2.0.443; R Core Team, Vienna, Austria). Significance was defined using a 2-sided *P* value of ≤.05. Receiver operating characteristic (ROC) curve analyses were performed for each outcome measure to generate optimal cutoff values for CVR at each point of interest using Youden's index.

Results

Patient characteristics

There were 123 of 125 patients who fit our inclusion criteria for isolated CLM, 54 from site A (43.9%) and 69 (56.1%) from site B. Fetuses with additional significant birth defects, namely congenital diaphragmatic hernia (n=1) or severe congenital cardiac disease (n=1), were excluded from further analysis. Of the included fetuses, 63% were male. The mean initial CVR was 0.67±0.61 cm^2 at 22.9±3.9 weeks' gestation. The mean maximum CVR was 1.08±0.94 cm^2 at 27.0±4.0 weeks' gestation. The mean final CVR was 0.58±0.60 cm^2 at 33.2±4.1 weeks' gestation.

Prenatal treatment

A total of 34 (27.6%) fetuses were subjected to maternal steroid administration to prevent or treat hydrops. Eight (6.5%) had documented hydrops, and 4 (3.3%) underwent invasive fetal intervention. Two had

TABLE 2
Multivariable regression of initial CVR and other prenatal factors on neonatal outcome in fetal lung malformations

A. Neonatal resection

Variable	Coefficient	SE	*P*
Gestational age at delivery (wk)	−0.21	0.12	.091
Maternal steroids	1.57	0.86	.068
Hydrops	−0.32	2.12	.879
Fetal operation	16.83	2068.64	.994
Initial CVR	2.83	0.96	.003[a]

B. Supplemental O_2

Variable	Coefficient	SE	*P*
Gestational age at delivery (wk)	−0.61	0.18	.005[a]
Maternal steroids	1.05	0.69	.125
Hydrops	1.33	1.30	.307
Fetal operation	15.07	2236.66	.995
Initial CVR	1.98	0.82	.015[a]

C. Endotracheal intubation

Variable	Coefficient	SE	*P*
Gestational age at delivery (wk)	−0.36	0.16	.026[a]
Maternal steroids	2.53	1.48	.087
Hydrops	0.73	2.45	.765
Fetal operation	−1.69	2.58	.513
Initial CVR	5.02	1.79	.005[a]

CVR, congenital pulmonary airway malformation volume ratio; *SE*, standard error.

[a] Indicates a *P* value of ≤.05.

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thoracoamniotic shunts, 1 received in utero sclerotherapy with drainage of a fetal hydrothorax, and 1 had an ex utero intrapartum treatment procedure. Fetuses who were subjected to maternal steroids had significantly higher initial (1.11±0.79 cm^2 vs control: 0.50±0.42 cm^2; *P*<.001), maximum (1.92±1.13 cm^2 vs control: 0.75±0.60 cm^2; *P*<.001), and final (0.93±0.70 cm^2 vs control: 0.44±0.50 cm^2; *P*<.001) CVRs. Similarly, hydropic fetuses had significantly higher CVRs at each time point (initial: 1.79±1.23 cm^2 vs control: 0.60±0.47 cm^2; *P*=.042; maximum: 3.16±1.75 cm^2 vs control: 0.97±0.75 cm^2; *P*=.028; final: 1.73±0.88 cm^2 vs control: 0.51±0.50 cm^2; *P*=.01).

Postnatal course

The mean gestational age at delivery was 38.3±2.6 weeks' gestation. A total of 24 (19.5%) neonates were managed with supplemental O_2, 12 (9.8%) required endotracheal intubation, and 15 (12.2%) underwent neonatal lung resection. All 15 fetuses who required neonatal resection had tachypnea and/or were placed on supplemental O_2 at birth (Figure 1). The mean postnatal age at neonatal surgery was 5.9±8.5 days. All 3 measures of respiratory morbidity were associated with significantly higher initial, final, and maximum CVRs (Table 1). Multivariable logistic regression based on CVR and prenatal indicators of disease severity, namely gestational age, maternal steroids, fetal hydrops, and fetal operation, revealed that CVR and gestational age at delivery were the only 2 variables significantly associated with neonatal resection, supplemental O_2, and endotracheal intubation (Tables 2–4).

Given that all 3 CVR measurements were significant in multivariable regression analyses after adjusting for hydrops and maternal steroid use, we established optimal cutoffs for predicting adverse neonatal outcomes (Table 5). Although there was only modest diagnostic accuracy of optimal CVR cutoff points for predicting the need for supplemental O_2, there was excellent discrimination (area under the curve [AUC] >0.85) for endotracheal intubation and neonatal resection based on initial, final, and maximum CVR cutoff values. An initial CVR ≥0.80 cm^2 was associated with a neonatal resection positive predictive value (PPV) and negative predictive value (NPV) of 32% and 98%, respectively. A maximal CVR ≥1.5 cm^2 was associated with a PPV of 48% and an NPV of 100% for neonatal resection. A final CVR ≥1.3 cm^2 was associated with the highest overall diagnostic accuracy based on a high specificity and PPV (82%–100%) for both the primary and secondary outcome measures, as well as high sensitivity and NPV (89%–97%).

Discussion

The initial CVR was first described more than 20 years ago as a sonographic measurement tool for assessing the risk for fetal hydrops and the need for prenatal surgery.[10] More recently, a seminal study published in the American Journal of Obstetrics & Gynecology described the use of serial CVR measurements as a predictor for identifying the 10% to 20% of nonhydropic fetuses who will nevertheless be symptomatic at birth and will require early lung surgery.[7] Although subsequent single-center studies in the United States and elsewhere have corroborated these findings,[12,19,20,24] there has been less consensus on the validity and implementation of CVR values for predicting

TABLE 3
Multivariable regression of maximum CVR and other prenatal factors on neonatal outcome in fetal lung malformations

A. Neonatal resection

Variable	Coefficient	SE	*P*
Gestational age at delivery (wk)	−0.35	0.16	.026[a]
Maternal steroids	1.51	1.19	.203
Hydrops	−1.38	1.66	.405
Fetal operation	13.81	3050.65	.996
Maximum CVR	3.24	0.97	<.001[a]

B. Supplemental O_2

Variable	Coefficient	SE	*P*
Gestational age at delivery (wk)	−0.51	0.15	<.001[a]
Maternal steroids	0.90	0.75	.229
Hydrops	1.34	1.47	.365
Fetal operation	15.37	2042.11	.994
Maximum CVR	0.93	0.46	.046[a]

C. Endotracheal intubation

Variable	Coefficient	SE	*P*
Gestational age at delivery (wk)	−0.44	0.16	.006[a]
Maternal steroids	1.01	1.16	.384
Hydrops	−0.72	1.62	.657
Fetal operation	−3.49	2.09	.096
Maximum CVR	2.91	0.93	.002[a]

CVR, congenital pulmonary airway malformation volume ratio; *SE*, standard error.

[a] Indicates a *P* value of ≤.05.

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neonatal outcomes.[13] Accordingly, recent studies suggest that many maternal-fetal medicine providers do not routinely obtain any CVR measurements, perhaps based on a perception of lack of use in management planning.[23,25]

Principal findings and results

In this study, we performed a comparative analysis of the initial CVR, maximum CVR, and final CVR and found that all of them were significantly associated with the rates of neonatal lung surgery in patients with prenatally diagnosed fetal lung lesions. In contrast, the use of maternal steroids and hydrops were not independently associated with neonatal surgical outcome. Neonatal lung resection was chosen as the primary outcome measure because the procedure addresses mass effect on the cardiopulmonary system and would likely be most specific for differentiating CLM newborns with symptomatic vs asymptomatic disease. The mean age at neonatal resection was approximately 6 days, a figure that is consistent with the reported literature.[21,26] Using the Pediatric Health Information System database to study 256 neonates with symptomatic CLMs, approximately 1 in 6 (17%) underwent lung resection within 24 hours of life.[26]

In this study, we also found that all 3 CVR measurements were associated with other neonatal respiratory morbidity measures, including supplemental O_2 and mechanical ventilation within the first 24 hours of life. In an era in which fetuses without hydrops with larger microcystic CPAMs are often managed with maternal steroids in an attempt to lower subsequent CVR measurements,[17,25,27] we were able to adjust for steroid administration and other fetal interventions in the analysis. Almost 28% of patients in our series received maternal steroids, a figure that is approximately twice the rate when compared with that in other contemporary studies.[4,28,29] Unsurprisingly, gestational age at delivery was the only other prenatal risk factor that was associated with neonatal respiratory morbidity.[17]

TABLE 4
Multivariable regression of final CVR and other prenatal factors on neonatal outcome in fetal lung malformations

A. Neonatal resection

Variable	Coefficient	SE	*P*
Gestational age at delivery (wk)[a]	−0.14	0.19	.455
Maternal steroids	3.80	2.50	.128
Hydrops	−0.26	1.78	.886
Fetal operation	19.76	2491.52	.994
Final CVR[b]	3.96	1.29	.002[c]

B. Supplemental O_2

Variable	Coefficient	SE	*P*
Gestational age at delivery (wk)[a]	−0.51	0.15	<.001[c]
Maternal steroids	1.28	0.72	.074
Hydrops	1.63	1.46	.262
Fetal operation	16.71	1558.67	.992
Final CVR[b]	1.50	0.54	.005[c]

C. Endotracheal intubation

Variable	Coefficient	SE	*P*
Gestational age at delivery (wk)[a]	−0.28	0.15	.055
Maternal steroids	1.98	1.23	.106
Hydrops	1.16	1.51	.441
Fetal operation	1.16	1.81	.521
Final CVR[b]	2.80	0.79	<.001[c]

CVR, congenital pulmonary airway malformation volume ratio; *SE*, standard error.

[a] For gestational age, each additional week in utero impacts the likelihood of the outcome by the associated coefficient; [b] For CVR, each increase of 1.0 impacts the likelihood of the outcome by the associated coefficient; [c] Indicates a *P* value of ≤.05.

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Our study also identified CVR cutoff values that were highly correlated with our primary and secondary outcomes. The initial, maximum, and final CVR values were accurate in terms of predicting a need for neonatal resection and early intubation (AUC, 0.89−0.97). As expected, the CVR thresholds varied based on gestational age when measured because approximately two-thirds of CLMs nearly double in size until 25 to 27 weeks' gestation, followed by regression during the third trimester.[15,18] Neonatal surgery was associated with an initial CVR ≥0.8 cm^2, a maximum CVR ≥1.5 cm^2, and a final CVR ≥1.3 cm^2. Maximum CVR had maximum sensitivity because all patients who underwent resection had a maximum CVR above the cutoff. Our CVR cutoff values for neonatal surgery are consistent with those reported in previous studies, which ranged between 0.75 and 1.7 cm^2 for CVR thresholds.[25,30,31] Potential explanations for these different CVR results may be related to the smaller sample size, single-center referral bias, use of a composite outcome variable that included subsequent infectious complications, and analysis restricted to operative resection cases only.

Based on our initial CVR data when measured at a mean of 23 weeks' gestation, we found that having an initial CVR of <0.8 suggests a very high likelihood of not requiring neonatal resection for symptomatic disease. The CVR cutoff is nearly identical to that of a recent multicenter study based on operative registry data.[25] Those fetuses below the initial CVR threshold value of 0.8 cm^2 are at very low risk for neonatal resection or mechanical ventilation based on a negative predictive value of 98%. The relative inaccuracy of the CVR for determining supplemental O_2 requirement in neonates with a CLM has been demonstrated in a large prospective study and may also be secondary to more subjective indications for administering this supportive measure across different neonatology care settings.[18] Although our models to predict supplemental O_2 requirement were

TABLE 5
Diagnostic accuracy of optimal CVR cutoff values on neonatal outcomes in prenatally diagnosed lung malformations

A. Neonatal resection

	Initial CVR ≥0.80	Maximum CVR ≥1.50	Final CVR ≥1.30
AUC (95% CI)	0.89 (0.81–0.97)	0.97 (0.94–1.00)	0.93 (0.85–1.00)
Sensitivity	0.86	1.00	0.79
Specificity	0.77	0.87	1.00
PPV	0.32	0.48	1.00
NPV	0.98	1.00	0.97

B. Supplemental O_2

	Initial CVR ≥0.75	Maximum CVR ≥1.39	Final CVR ≥1.28
AUC (95% CI)	0.73 (0.60–0.87)	0.74 (0.59–0.89)	0.72 (0.59–0.86)
Sensitivity	0.70	0.68	0.48
Specificity	0.72	0.84	1.00
PPV	0.37	0.48	1.00
NPV	0.91	0.92	0.89

C. Endotracheal intubation

	Initial CVR ≥0.97	Maximum CVR ≥1.50	Final CVR ≥1.28
AUC (95% CI)	0.94 (0.87–1.00)	0.94 (0.87–1.00)	0.93 (0.86–1.00)
Sensitivity	0.82	0.91	0.75
Specificity	0.86	0.84	0.98
PPV	0.38	0.37	0.82
NPV	0.98	0.99	0.97

AUC, area under the curve; *CI*, confidence interval; *CVR*, congenital pulmonary airway malformation volume ratio; *NPV*, negative predictive value; *PPV*, positive predictive value.

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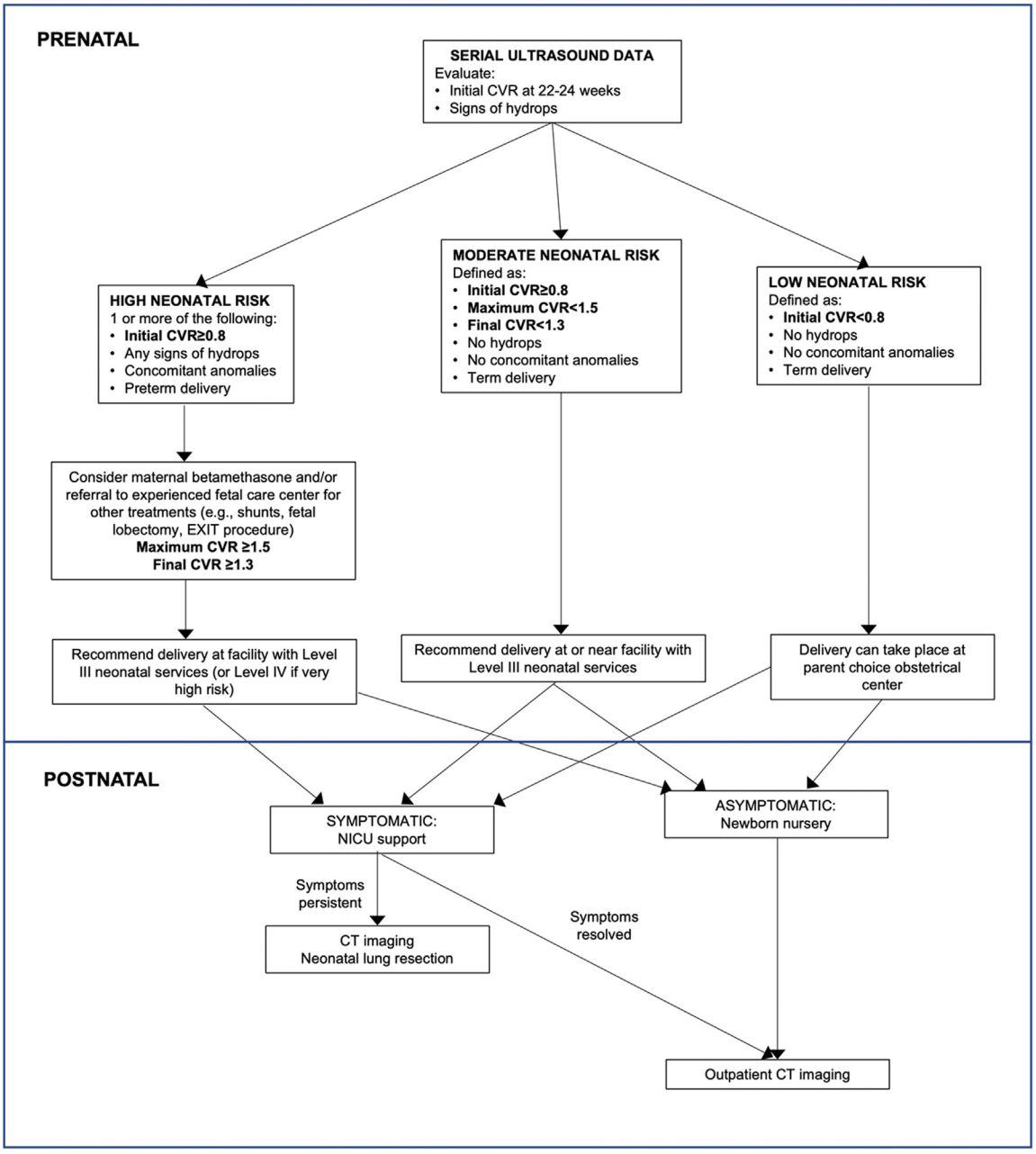
similarly not as robust as predicted for neonatal surgery, the negative predictive value associated with the initial CVR threshold of 0.8 cm^2 was still in excess of 90%.

Lastly, our results suggest that, among the different CVR measurements during pregnancy, the final CVR at approximately 33 weeks' gestation has maximal specificity for predicting neonatal lung resection. This time point is of critical important because it allows adjustment of perinatal management based on this measurement. A final CVR >1.3 cm^2 was predictive of symptomatic disease in 82% of cases in contrast with much lower PPVs among CVRs measured earlier in gestation. The NPV remained high (97%) for both endotracheal intubation and neonatal resection. Although CVR measurements are adjusted for fetal head circumference, higher CVRs seem to be better tolerated later in gestation because the fetal thoracic cavity volume grows more rapidly than the mass volume in most cases based on the resolution of mediastinal shift and fetal magnetic resonance volumetry studies.[14] Historically, there has been some reluctance by maternal-fetal medicine providers to rely on CVR measurements in the third trimester because of the known loss of echogenicity and resolution of mediastinal shift in many CLMs late in gestation.[32] These concerns, however, are not supported by our data or by other studies that have demonstrated the value of third trimester CVRs in predicting postnatal outcome.[7,21,33]

Clinical implications

Taken together with the current literature, our results strengthen the case for CVR-based management algorithms to help with prenatal counseling, ultrasound surveillance, and delivery planning. A suggested algorithm is shown in Figure 2. If the initial CVR between 22 and 24 weeks' gestation is less than 0.8 cm^2, there is a low likelihood of requiring neonatal lung surgery owing to symptomatic disease. For those with an initial CVR greater than 0.8 cm^2, we would advocate for serial CVR measurements until 32 to 34 weeks' gestation to the obtain maximum and final CVRs. For final CVRs <1.3 cm^2, neonatal lung resection rates are less than 5%, and the risk-benefit of the child being delivered at a local obstetrical

FIGURE 2
Evidence-based management algorithm for fetal pulmonary malformations



CT, computed tomography; *CVR*, congenital pulmonary airway malformation volume ratio; *EXIT*, ex utero intrapartum treatment; *NICU*, neonatal intensive care unit.

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unit without level III neonatal intensive care facilities and pediatric surgical support can be discussed with families. Conversely, fetuses with subsequent CVRs equal ≥1.3 cm^2 are at much higher risk for respiratory compromise at birth and ought to be delivered at a hospital with immediate access to neonatal intensive care and surgical expertise.

Strengths and limitations

Despite the aforementioned strengths of our study for prenatal counseling purposes, there are some limitations that warrant mention. First, our study is retrospective in nature and therefore subject to issues associated with data collection. We acknowledge that quantifying mild respiratory distress and the decision to use supplemental O_2 during the neonatal resuscitation can be subjective and that other causes of respiratory morbidity (eg, prematurity, transient tachypnea of

the newborn) could explain symptomatology. Our study also did not account for potential confounders such mediastinal shift, polyhydramnios, macrocystic disease, the presence of a systemic feeding vessel, and pathologic diagnosis. Based on work from other investigators, it is unlikely that most of these variables would be independent risk prognosticators of neonatal outcome.[9,16,18,31] Finally, the external validity of our suggested CVR thresholds may be restricted to larger maternal-fetal referral centers because the exact CVR cutoff values may differ across institutions because of local ultrasound expertise. Although the results from some studies have suggested lower CVR cutoffs for neonatal risk stratification,[18,30,34] others from the United States and Japan concur with our proposed threshold values associated with surgical intervention.[20,33,35]

Research implications

Future studies should focus on validating these results within a large, prospective, international registry to obtain a better understanding of the interrater reliability of CVR measurements and to evaluate the potential impact of fetal magnetic resonance imaging as a complementary study in the management of these patients.[29,36,37]

Conclusion

This multicenter study highlights the potential value of determining the CVR in the third trimester for perinatal risk stratification and decision-making for patients with congenital pulmonary lesions. Despite the widespread use of maternal steroids in the management of larger fetal lung lesions, CVR values at any time in pregnancy, but especially CVRs later in gestation, are highly predictive of a symptomatic neonatal course that ultimately requires early lung resection. Third trimester CVRs $\geq$1.3 cm^2 confer a high risk for respiratory compromise at birth, and the delivery of such cases at birthing centers with immediate access to advanced neonatal intensive care support and pediatric surgical expertise is suggested. ■

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajogmf.2023.101128.

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