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RESEARCH ON THE PREDICTIVE VALUE OF PULMONARY VEINS PULSATILITY INDEX AND MAIN PULMONARY ARTERY DOPPLER INDICES IN FETAL GROWTH RESTRICTION

SUMMARY OF THE PH.D. THESIS IN MEDICINE

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INTRODUCTION

Fetal growth restriction is the term used to describe fetal growth that falls below the fetal potential because of pathological reasons. Fetal growth restriction, which occurs in 3% - 7% of pregnancies, is the leading cause of stillbirth, neonatal mortality, and diseases. Over the last three years, prestigious federations and obstetric-gynecological societies have released the most up-to-date guidelines for clinical practice regarding fetal growth restriction. The fetal pulmonary circulation constitutes just 21% of the whole cardiac output. However, changes in Doppler indices have been detected in both the pulmonary veins and pulmonary arteries when the fetus has restricted growth. Specifically, the pulsatility indices of the pulmonary venous and pulmonary artery in fetuses with growth retardation exhibited an increase as compared to fetuses with normal growth.

Nevertheless, the guidelines stated earlier do not include any information about the significance of Doppler in fetal pulmonary circulation for managing fetal growth restriction. There is no published information about whether Doppler changes in the pulmonary circulation of growth-restricted fetuses have extra predictive value for fetal health or newborn outcomes. Hence, we conducted a study titled "*Research on the predictive value of pulmonary vein pulsatility index and main pulmonary artery Doppler indices in fetal growth restriction*" with the dual objectives:

1. *Evaluate the pulmonary vein pulsatility index and pulmonary artery Doppler indices in fetuses with normal growth and restricted growth fetuses.*

2. *Investigate the predictive significance of the pulmonary vein pulsatility index and the pulmonary artery Doppler indices for the health of growth-restricted fetuses at both the fetal and newborn stages.*

NEW CONTRIBUTION OF THE THESIS

No studies in Vietnam have established reference intervals for the fetal pulmonary vein and pulmonary artery Doppler indices. Research on the influence of pulmonary vein pulsatility index and pulmonary artery Doppler indices in growth-restricted fetuses on fetal and neonatal health prediction remains relatively rare worldwide. The findings of this research provided a reference range for pulmonary vein and pulmonary artery Doppler indices in adequately growing fetuses. Furthermore, the pulmonary vein pulsatility index has predictive relevance for fetal umbilical artery blood pH and adverse neonatal outcomes in growth-restricted fetuses. At the same time, the pulmonary artery AT/ET ratio predicts neonatal respiratory distress in growth-restricted fetuses. The research used the cutoff point and percentile to determine the Doppler indices's diagnostic and predictive significance, as mentioned above, for fetal and neonatal health in growth-restricted fetuses.

THESIS STRUCTURE

The thesis is structured 123 pages as follows: Introduction (02 pages), Literature Review (25 pages), Subjects and Methodology of the research (23 pages), Research results (34 pages), Discussion (36 pages), Conclusion (02 pages), and Proposal (1 page). The thesis incorporates various visual aids such as 35 tables, 30 charts, and 17 drawings, along with 187 reference papers in Vietnamese (13 articles) and English (174 articles). An appendix (8 pages) is also included. The study has yielded ten projects published in major medical publications and conferences, both locally and abroad.

CHAPTER 1: LITERATURE REVIEW

1.1 DEFINITION AND CLASSIFICATION OF FETAL GROWTH RESTRICTION

Fetal growth restriction is a medical condition in which a fetus does not reach all of its growth potential owing to pathological causes, which typically involve placental malfunction. In clinical practice, estimated fetal weight or abdominal circumference below a given threshold, such as the 10th or 3rd percentile, is often used to identify fetuses at risk of growth restriction.

Studies recommend expanding the categorization of fetal growth restriction based on gestational age at diagnosis to include early-onset (<32 weeks) and late-onset (≥32 weeks).

1.2 ETIOLOGY OF FETAL GROWTH RESTRICTION

Causes of fetal growth restriction are classified into three groups: fetus, mother, and placenta-related.

1.3.PATHOGENESIS OF FETAL GROWTH RESTRICTION

The pathophysiology is unclear. However, hypoperfusion of the placenta impairs nutrition transfer to the fetus and induces fetal growth restriction.

1.4. RISKS OF PREGNANCY WITH FETAL GROWTH RESTRICTION

Risks for fetal growth restriction include fetal problems and obstetric complications. Fetal growth restriction with accompanying abnormalities increases the risk of adverse perinatal outcomes, such as needing three times more respiratory assistance and ten times more mechanical ventilation than in instances without abnormalities.

1.5. EARLY PREDICTION OF FETAL GROWTH RESTRICTION

There is presently no test that can accurately predict fetal growth restriction. As a result, the routine application of fetal growth restriction prediction models should be considered with caution.

1.6. DETECTING FETAL GROWTH RESTRICTION

Assessing fetal growth through measuring fetal biometrics during a single ultrasound is routine clinical practice, even though a single fetal ultrasound can only identify size and can not inspect the fetus. Currently, the most precise approach for evaluating fetal size is to estimate fetal weight. In clinical practice, fetal growth restriction is often defined as a combination of fetal biometrics and aberrant blood flow Doppler findings.

1.7. MANAGEMENT OF FETAL GROWTH RESTRICTION

1.7.1 Management of early-onset fetal growth restriction

An evidence-based agreement exists on diagnostic, monitoring, and delivery timing for early-onset fetal growth restriction. In addition to maternal birth indications, delivery indications are examined based on CTG, computerized CTG, biophysical profile, and Doppler of the ductus venous and umbilical artery.

1.7.2 Management of late-onset fetal growth restriction

Late-onset fetal growth restriction is responsible for 50% of stillbirths. The umbilical artery Doppler, CTG, and computerized CTG are now used to determine the delivery time rather than the ductus venosus.

1.7.3 Time of delivery

The gestational age, severity, and signals detected during monitoring of the growth-restricted fetus and the mother's symptoms are used to determine the delivery timing.

1.8 MEDICAL INTERVENTIONS

When a fetus is at risk of premature delivery, corticosteroids are administered to mature the fetal lung. The optimality of this prophylactic method is achieved when the treatment course is carried out between 2-7 days before giving birth.

Magnesium sulfate treatment in pregnant women at risk of preterm delivery has been demonstrated to have neuroprotective effects on the newborn, lowering the risk of perinatal mortality, cerebral palsy, and gross motor impairments.

Several trials are being conducted to evaluate the potential of resolving perfusion deficiencies between the uterus and the placenta. However, no intervention method has been successful for instances of fetal growth restriction.

1.9. CHARACTERISTICS OF HEART AND LUNGS IN FETAL GROWTH RESTRICTION

Increased myocardial performance index was found in early-onset fetal growth restriction cases from the 24th week of pregnancy. However, this does not represent an improvement in myocardial performance due to prolonged systolic relaxation time. Fetal cardiac dysfunction also increases from 35 weeks gestation in cases of late-onset fetal growth restriction with manifestations such as an enlarged heart and more spherical shape. At the same time, signs of cardiac dysfunction also appear, which include abnormalities of the systolic relaxation phase.

Pulmonary complications caused by intrauterine growth restriction have not been uniformly described. This may stem from differences between individuals with intrauterine growth restriction due to different etiologies. However, clear evidence from many studies has shown that chronic hypoxia is associated with disruption of lung development in growth-restricted fetuses. At the same time, respiratory system injuries are also likely to occur in the postpartum period.

1.10. SEVERAL STUDIES INVESTIGATING THE CORRELATION BETWEEN DOPPLER INDICES OF THE FETAL PULMONARY CIRCULATORY SYSTEM AND PREGNANCY OUTCOMES IN FETAL GROWTH RESTRICTION HAVE BEEN PUBLISHED

1.10.1 Fetal main pulmonary artery pulsatility index

Research by Sun L. and colleagues has demonstrated a correlation between oxygen in the fetal blood at birth and flow in the fetal pulmonary artery in late-stage fetuses with growth retardation. Reduced flow and changes in the flow velocity waveforms in pulmonary artery branches can be early signs of fetal distress. In addition, it occurs before the change in the pulsatility index of the middle cerebral artery.

Prospective research by Hosseinzadeh R. and colleagues showed that the pulmonary artery pulsatility index in fetuses with growth restriction was higher than in the group of fetuses with appropriate growth. For the fetal growth restriction group, a pulmonary artery pulsatility index above the 95th percentile was associated with infants needing treatment in the NICU due to respiratory problems. Additionally, 100% of newborns in this group required oxygen therapy. Pulmonary artery Doppler ultrasound can provide the necessary predictions to reduce mortality and morbidity in infants with growth-restricted pregnancies.

1.10.2 Fetal pulmonary veins pulsatility index

Bravo-Valenzuela and colleagues' research shows that the pulmonary venous pulsatility index of growth-restricted fetuses is increased and reflects a decrease in left ventricular compliance and a change in left atrial activity.

Lee and Cho's research determined the cutoff point to be 1.13 of the pulmonary vein pulsatility index, which has a predictive value for small gestational age fetuses with a sensitivity of 70.27% and a specificity of 92.3%, a positive predictive value of 78.79% and a negative predictive value of 88.54 %. In addition, the area under the ROC curve of the pulmonary vein pulsatility index for predicting small gestational age fetuses had no difference from the estimated fetal weight percentile index.

CHAPTER 2
SUBJECTS AND METHODS OF RESEARCH

2.1 RESEARCH SUBJECTS

2.1.1 Subjects, location, and time of study: 420 singleton pregnancies (210 fetuses with restricted growth and 210 fetuses with appropriate growth) came for examination and treatment at Da Nang Hospital for Women and Children from June 2017 to December 2021

2.1.2 Disease selection criteria

*2.1.2.1 General criteria of two group*s (fetal growth restriction group and fetal appropriate growth group): gestational age between 28 weeks - 40 weeks, the fetus has no morphological abnormalities, estimated fetal weights were calculated using the Hadlock-4 formula on fetal ultrasound, the percentile of the estimated fetal weight on ultrasound and the baby's weight immediately after birth are compared with the Hadlock-4 reference table, the values of Doppler index of the umbilical artery, cerebro-placental ratio are classified as abnormal or normal according to the New-Zealand Obstetric Ultrasound Guidelines, fetuses with two-dimensional ultrasound and pulsed Doppler ultrasound results within only 48 hours before birth were selected for the research sample and agreed to participate in the study.

2.1.2.2 Specific criteria for the fetal growth restriction group (case group): estimated fetal weight on ultrasound below 3^{rd} percentile; or estimated fetal weight between 3^{rd} percentile to below 10^{th} percentile combined umbilical artery pulsatility index above 95th percentile; or estimated birth weight between 3^{rd} percentile to below 10^{th} percentile combined with cerebro-placental ratio below 5^{th} percentile. Fetal weight after birth is in accordance with the classification of the prenatal period.

2.1.2.3 Specific criteria for the fetal appropriate growth group (control group): Healthy pregnant women, no history of metabolic - autoimmune - cardiovascular diseases, no respiratory or cardiovascular diseases, no hypertension, urinary, and autoimmune during pregnancy, estimated fetal weight on prenatal ultrasound and postnatal fetal weight ranged from 10^{th} percentile to 90^{th} percentile, normal umbilical artery Doppler and cerebro-placental ratio values.

2.1.3 Exclusion criteria: It is crucial to note that participants were excluded if there was no estimated date of delivery based on the gestational age of 8 weeks - 10 weeks or if it was impossible to collect all the variables that needed to be researched. This could be due to factors such as the mother's abdominal wall being too thick, polyhydramnios, or insufficient data on variables that need to be collected postpartum.

2.2 RESEARCH METHODS

2.2.1 Research design: The study used a prospective, paired cohort method. The matching process is performed when there is an indication for delivery, in which the matching is selected between the gestational age of the disease group and the gestational age of the control group.

2.2.2 Sample size:

- *Estimated sample size for the first objective:* As per convention, at least 120 healthy pregnancies are required to establish reference value ranges for fetal pulmonary vein and pulmonary artery Doppler indices. For the second objective, there were 210 fetuses with growth restriction. Hence, this study included 210 fetuses with appropriate growth that met the disease selection criteria. This was to ensure a robust investigation and establishment of the reference range of the fetal pulmonary vein and pulmonary artery Doppler indices.

- *Estimated sample size for the second objective*: formula to calculate sample size for selected diagnostic test:

$$n(spe) = \frac{TN + FP}{1 - P}$$ and $$TN + FP = \frac{Z_{1-\frac{\alpha}{2}}^{2} * Spe * (1 - Spe)}{d^2}$$

In which *n(spe)* represents the number of sample sizes calculated by specificity; TN is the number of true negatives; FP is the number of false positives; Spe is the specificity (Spec = 93%); d is the variation of specificity with 95% confidence interval (d = 0.05); $Z1-\alpha/2$ is the statistical significance level 5% ($Z1-\alpha/2$ = 1.96), and P is the disease incidence (P = 0.32). Applying this formula, the minimum sample size for the second objective is 142 fetuses with growth restriction. This study had 210 growth-restricted fetuses that met the inclusion and exclusion criteria.

2.2.3 Research tools: printed data collection form, obstetric medical records, TANTA adult scale, INFANT SCALE newborn scale, reference table for estimated fetal weight on ultrasound according to Hadlock, machine GE Volusion S6 ultrasound (convex abdominal probe with frequency 3.5 - 6 MHz), Monitoring BT-350 machine, GASTAT 1835 blood gas testing machine (Serial number 0128202).

2.2.4 Procedures

2.2.4.1 Interviewing common characteristics

2.2.4.2 Exploiting historical and medical history factors related to disease selection criteria and exclusion criteria

2.2.4.3 Exploiting characteristics of pregnant women before pregnancy: height, weight, BMI, BMI classification.

2.2.4.4 Clinical examination of pregnant women in the current pregnancy: determine gestational age, measure pulse and blood pressure, calculate weight gained during pregnancy, classify weight gain

2.2.4.5 Two-dimensional ultrasound: Collect biometric measurements of the head, abdomen, and femur length to estimate fetal weight, evaluate the characteristics of the placenta and amniotic fluid, and survey the morphology of the fetus to rule out cases of congenital structural abnormalities.

2.2.4.6 Pulsed Doppler ultrasound: Step 1-Survey and classify the umbilical artery, middle cerebral artery, and ductus venosus pulsatility index. Step 2-Calculate the cerebro-placental ratio. Step 3-Investigating Doppler blood flow indices in the fetal pulmonary veins, including peak systolic velocity, peak diastolic velocity, end-diastolic velocity, peak velocity index, and pulse index. Step 4-Investigating Doppler blood flow indices in the fetal pulmonary main artery, including peak systolic velocity, pulse index, acceleration time, ejection time, and the ratio between acceleration time and ejection time.

2.2.4.7 Recording and classifying CTG: according to the criteria proposed by the International Federation of Gynecology and Obstetrics in 2015.

2.2.4.8 Pregnancy monitoring and management: The group of fetuses with appropriate growth are monitored for labor or delivery according to indications from the mother and fetus. The group of fetuses with restricted growth was monitored and treated according to a specific protocol. Cases with a gestational age before 34 weeks are supplemented with a course of lung maturation with Corticosteroids if the pregnancy has not been treated before. In addition, Magne Sulfate treatment is also added for pregnancies with a gestational age of less than 32 weeks.

2.2.4.9 Collecting data at the end of pregnancy: All results of the two groups are collected, especially ultrasound data taken from the last time performed, and must be within 48 hours before birth. Collected data include gestational age at delivery, birth method, umbilical artery blood pH, newborn's sex, Apgar scores at the first and fifth minutes, fetal weight at birth, neonatal transfer to a neonatal intensive care unit, neonatal respiratory distress, causes of neonatal respiratory distress, adverse neonatal outcomes.

2.3 DATA COLLECTION AND PROCESSING

The collected data are meticulously recorded on data collection sheets, and the analysis is performed using SPSS version 20 and Medcalc version 20.1. The statistical algorithms used in this study, including percentage calculation, statistical estimation, and testing of statistically significant hypotheses with $p < 0.05$, are all crucial components of our robust methodology. These techniques, along with others such as relative risk, correlation coefficient, Pearson correlation (r), sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, positive predictive value, and negative predictive value, are all instrumental in our research. We also evaluate the usefulness of a diagnostic method using ROC curve analysis and compare the area under the curve (AUC) of diagnostic methods to test for differences in diagnostic value.

Establishing the reference value range for pulmonary veins and pulmonary artery Doppler indices of fetuses growing normally according to gestational age and the limit values of the corresponding values at the 95^{th} percentile and 5^{th} percentile is a significant part of our study.

The multiple linear regression model estimates a dependent variable's value and builds a prediction model for umbilical artery blood pH in growth-restricted fetuses. Binary logistic regression analysis is applied to create a model to predict the likelihood of neonatal respiratory failure in fetal growth restriction.

2.4 RESEARCH ETHICS:

The research was approved by the Ethics Council in Biomedical Research of Hue University of Medicine and Pharmacy according to decision No. H2017/15, signed on April 28, 2017. The research was also approved by the Scientific and Technical Council of Da Nang Hospital for Women and Children, according to the Minutes signed on May 2, 2017.

CHAPTER 3
RESEARCH RESULTS

3.1 GENERAL CHARACTERISTICS OF THE RESEARCH SAMPLE

3.1.1 Common characteristics of the two research groups

The average age of mothers in the fetal growth restriction group was 30.01 ± 5.75, and the normal fetal growth group was 29.72 ± 5.69 ($p > 0.05$). The difference between the case and control groups was insignificant ($p > 0.05$) when considering BMI classification and maternal weight gain. The difference in the number of pregnant women with C-sections was also not statistically significant between the two groups ($p > 0.05$). The average gestational age at the end of pregnancy in the case group is 35.71 ± 2.35 (weeks), and the control group is 35.47 ± 2.60 (weeks); the difference is not statistically significant ($p > 0.05$).

3.1.2 Characteristics of pregnancy with fetal growth restriction

This study's severe fetal growth restriction rate accounted for 65.7% of the disease group. The rate of fetal growth restriction after 32 weeks accounts for 91.4% of the disease group. The risk of cesarean section in the group with restricted growth is higher than the group with normal growth with OR: 3.76; 95% CI: 2.32 – 6.09; $p < 0.0001$.

3.1.3 Characteristics of pregnancy outcomes according to fetal growth classification

The neonatal weight of the disease group at birth was 1959 ± 410 grams, and that of the control group was 2493 ± 651 grams. Mean Apgar scores at 1 minute and 5 minutes were 7.12 ± 1.20 and 7.84 ± 1.21, respectively; and in the control group, it was 7.53 ± 1.01 and 8.39 ± 0.93, respectively. The umbilical artery blood pH immediately after the group's birth with restricted growth was 7.22 ± 0.04, and the group with normal growth was 7.26 ± 0.02. The indicators mentioned above in the group of fetuses with restricted growth were all lower than those with normal growth, and the difference was statistically significant ($p < 0.001$).

Fetal growth restriction increases the risk of adverse neonatal outcomes by 1.97 times (95% CI: 1.33 - 2.91; $p < 0.001$). In particular, the risk of Apgar at 1 minute < 7 points is 2.45 times (95% CI: 1.46 - 4.10; $p < 0.001$), the risk of Apgar at 5 minutes < 7 points is 5 .76 times (95% CI: 2.62 – 12.65; $p < 0.001$); The risk of transfer to a neonatal intensive care unit is 1.55 times (95% CI: 1.05 - 2.30; $p < 0.05$) and the risk of umbilical artery blood pH < 7.20 is 153.95 times ($p < 0.001$).

When compared with the group with fetal growth restriction with weight above the 3rd percentile, the group with severe fetal growth restriction is more likely to have a low Apgar score and transfer the newborn to the NICU for treatment ($p < 0.01$).

3.1.4 Characteristics of the umbilical artery pulsatility index

The umbilical artery pulse index of fetuses with growth retardation is higher than that of fetuses with normal growth (1.13 ± 0.27 compared to 0.91 ± 0.13). In both study groups, fetuses with adverse neonatal outcomes had higher umbilical artery pulsatility index. These differences are statistically significant with $p < 0.001$.

Weak negative correlation between umbilical artery pulsatility index and umbilical artery blood pH in appropriate growing fetuses ($r = - 0.17$; $p < 0.05$). A strong negative correlation exists between the umbilical artery pulsatility index and umbilical artery blood pH in growth-restricted fetuses ($r = - 0.53$; $p < 0.001$).

The predictive value of the umbilical artery pulse index for adverse neonatal outcomes in growth-restricted fetuses is moderate (AUC = 0.768; $p < 0.001$).

3.1.5 Characteristics of cerebro-placental ratio and umbilico-cerebral ratio

Compared to the group with normal growth, the group with slow growth had a lower cerebro-placental ratio (1.22 ± 0.22 compared to 1.90 ± 0.28) and a higher umbilico-cerebral ratio (0.85 ± 0.20 vs. 0.54 ± 0.07), these differences are statistically significant with $p < 0.001$.

The cerebro-placental ratio has no significant predictive value for adverse neonatal outcomes in growth-restricted fetuses (AUC = 0.525; $p > 0.05$).

The umbilico-cerebral ratio has no significant predictive value for adverse neonatal outcomes in growth-restricted fetuses (AUC = 0.522; $p > 0.05$).

3.2 DOPPLER INDICES OF PULMONARY VEINS AND PULMONARY ARTERY IN FETAL APPROPRIATE GROWTH AND FETAL GROWTH RESTRICTION

3.2.1 Reference value range of pulmonary veins Doppler indices in normally growing fetuses

Table 3.10: Regression formula of Doppler indices of pulmonary veins according to gestational age

Parameter	Transformation	Constant (α)	Slope (β)	Significance
Peak systolic velocity (cm/s)	-	-26,420	1,749	< 0,001
Peak diastolic velocity (cm/s)	-	-26,01	1,64	< 0,001
End-diastolic velocity (cm/s)	-	-17,149	0,829	< 0,001
Peak velocity index	NL	0,101	-0,0064	< 0,001
Pulsatility index	NL	0,36	-0,0123	< 0,001

(NL: Natural Logarithm)

3.2.2 Reference value range of the main pulmonary artery's Doppler indices in normally growing fetuses

Table 3.11: Regression formulas for Doppler indices of fetal pulmonary main artery according to gestational age

Parameter	Transformation	Constant (α)	Slope (β)	Significance
Peak systolic velocity (cm/s)	NL	1,441	0,0132	< 0,001
Acceleration time (ms)	-	-16,292	1,630	< 0,001
Ejection time (ms)	-	92,478	2,331	< 0,001
AT/ET ratio	-	0,0244	0,006	< 0,001
Pulsatility index	NL	0,742	-0,00928	< 0,001

(NL: Natural Logarithm; AT: Acceleration Time; ET: Ejection Time)

3.2.3 Comparison of some Doppler indices of fetal pulmonary veins and main pulmonary artery between fetuses with normal growth and fetuses with growth retardation

Compared with fetuses with normal growth, the pulmonary vein pulsatility index of fetuses with restricted growth is higher (1.13 ± 0.21 compared to 0.85 ± 0.15); this difference is statistically significant with $p < 0.001$.

Compared with fetuses with normal growth, the pulmonary main artery's AT/ET ratio of fetuses with restricted growth was higher (0.237 ± 0.024 vs. 0.220 ± 0.032), $p < 0.001$.

Compared with fetuses with normal growth, the pulmonary main artery pulsatility index of fetuses with restricted growth was higher (2.73 ± 0.26 compared to 2.60 ± 0.29), $p < 0.001$.

3.3 PREDICTIVE VALUE OF PULMONARY VEIN PULSATILITY INDEX AND FETAL MAIN PULMONARY ARTERY DOPPLER INDICES FOR FETAL AND NEONATAL HEALTH IN FETAL GROWTH RESTRICTION

3.3.1 Predictive value of pulmonary vein pulsatility index for fetal and neonatal health in fetal growth restriction

3.3.1.1 Correlation between pulmonary vein pulsatility index and some parameters in fetal growth restriction

A strong positive correlation exists between the fetal pulmonary veins pulsatility index and the umbilical artery pulsatility index ($r = 0.59$; $p < 0.001$).

A moderate negative correlation exists between the fetal pulmonary vein pulsatility index and cerebro-placental ratio ($r = - 0.34$; $p < 0.001$).

A strong negative correlation exists between the fetal pulmonary vein pulsatility index and umbilical artery blood pH ($r = - 0.61$; $p < 0.001$).

3.3.1.2 Predictive value of fetal pulmonary vein pulsatility index for umbilical artery blood pH of fetal growth restriction

Diagnostic and predictive value of fetal pulmonary venous pulsatility index above the 95^{th} percentile for umbilical artery blood pH < 7.20 in fetal growth restriction:

- Sensitivity: 87.5% (95% CI: 75.9% – 94.8%)
- Specificity: 70.1% (95% CI: 62.2% - 77.2%)
- Positive predictive value: 51.6 % (95% CI: 45.0% - 58.0%)
- Negative predictive value: 93.9 % (95% CI: 88.5% - 96.8%)
- AUC: 0.78 (95% CI: 0.72 – 0.84)

3.3.1.3 Predictive Model of umbilical artery blood pH in fetal growth restriction

Multivariable linear regression model combining characteristics of gestational age, CTG, umbilical artery pulse index, and fetal pulmonary vein pulsatility index has the highest adjusted R^2 coefficient for predicting umbilical artery pH blood of fetuses with restricted growth ($R^2 = 0.615$; $p < 0.001$).

Table 3.16: Analysis of the role of variables in multivariable regression models to predict umbilical artery blood pH in fetal growth restriction (excerpt from part of table 3.16)

Model	Dependent Variable	Unstandardized Coefficient (β)	Standardized Coefficient (β)	t	Significance	Collinearity Statistics VIF
GA - CTG – UAPI - PVPI	*GA*	- 0,004	- 0,228	- 4,550	< 0,001	1,365
	CTG	- 0,026	- 0,458	- 9,665	< 0,001	1,225
	UAPI	- 0,059	- 0,371	- 6,776	< 0,001	1,632
	PVPI	- 0,064	- 0,312	- 5,173	< 0,001	1,988
	Constant	7,524		184,8	< 0,001	

(GA: Gestation Age; CTG: Cardio Toco Graphy; UAPI: Umbilical Artery Pulsatility Index; PVPI: Pulmonary Vein Pulsatility Index)

3.3.1.4 Predictive value of pulmonary vein pulsatility index for adverse neonatal outcomes in fetal growth restriction

The predictive value of the pulmonary vein pulsatility index for adverse neonatal outcomes in growth-restricted fetuses is moderate (AUC = 0.783; $p < 0.001$).

The AUC values of the pulmonary vein pulsatility index and the umbilical artery pulsatility index, 0.783 and 0.768 respectively, show no statistically significant difference in predicting adverse pregnancy outcomes in growth-restricted fetuses ($p > 0.05$).

3.3.2 Predictive value of pulmonary main artery Doppler indices for fetal and neonatal health in fetal growth restriction

3.3.2.1 Predictive value of pulmonary main artery Doppler indices for umbilical artery blood pH of fetal growth restriction

The predictive value of the pulmonary main artery's AT/ET ratio for umbilical artery blood pH < 7.20 is not good (AUC = 0.620; $p < 0.001$).

The pulmonary main artery pulsatility index has no predictive value for umbilical artery blood pH < 7.20 (AUC = 0.571; p > 0.05).

3.3.2.2 Diagnostic and predictive value of fetal pulmonary main artery's AT/ET ratio for neonatal respiratory distress

Diagnostic and predictive value of pulmonary main artery's AT/ET ratio below the 5th percentile for neonatal respiratory distress in fetal growth restriction:

- Sensitivity: 68.8% (95% CI: 57.2% – 78.9%)
- Specificity: 84.9% (95% CI: 77.7% - 90.6%)
- Positive predictive value: 72.6 % (95% CI: 63.3% - 80.3%)
- Negative predictive value: 82.5 % (95% CI: 77.0% - 86.8%)
- AUC: 0.77 (95% CI: 0.70 – 0.82)

3.3.2.3 Predictive model for neonatal respiratory distress in fetal growth restriction

Table 3.19: Variables in the logistic regression model for predicting neonatal respiratory distress in fetal growth restriction

Variable	Regression Coefficient	OR	95% CI	Significance
Gestation Age	- 0,672	0,51	0,39 – 0,65	< 0,0001
$\mathbf{C\ \frac{AT}{ET}}$	1,979	7,24	3,35 – 15,61	< 0,0001
Constant	22,637			

($\mathrm{C}\ \frac{\mathrm{AT}}{\mathrm{ET}}$: *Classify the ratio of Acceleration time / Ejection time according to the 5th percentile)*

CHAPTER 4
DISCUSSION

4.1 GENERAL CHARACTERISTICS OF THE STUDY SAMPLE

4.1.1 Common characteristics of the two study groups

4.1.1.1 Maternal age

The age of pregnant women in both the case and control groups was similar, with the case group averaging 30.01 ± 5.75 (years) and the control group at 29.72 ± 5.69 (years). This similarity in maternal age between the two study groups, as indicated by a non-statistically significant difference ($p = 0.603$; table 3.1), aligns with findings from both domestic and foreign studies, providing a solid baseline for our research.

4.1.1.2 mother's pre-pregnancy BMI and weight gain during pregnancy

The difference was not statistically significant between the case and control groups regarding the Mother's BMI classification before pregnancy and the mother's standard weight gain classification during pregnancy. According to research by Nguyen Tran Thao Nguyen and colleagues (2020), the average weight gain of the mother in the case group was 9.52 ± 4.35 (kg), which was lower than the control group's 13.58 ± 4.19 (kg).

4.1.1.3 Gestational age at the time of birth

Our study was designed using the method of matching according to gestational age between the case group and the control group at the time of delivery. In particular, the average gestational age of the case group is 35.71 ± 2.35 (weeks), and the control group is 35.47 ± 2.60 (weeks). The decision to deliver in the context of fetal growth restriction depends on many factors, of which gestational age plays an important role.

4.1.2 Relationship between delivery method with fetal growth classification

The results of our study show that fetal growth restriction is a risk factor for cesarean section with OR: 3.76; 95% CI: 2.32

– 6.09; $p < 0.0001$. The study by Wilk C. et al. showed that the risk of cesarean section due to fetal growth restriction doubled (with OR: 2.00; 95% CI: 1.78 - 2.25).

4.1.3 Compare pregnancy outcome characteristics between the two study groups

The average weight of children immediately after birth in the fetal growth restriction group (1959 ± 410 grams) was statistically significantly lower ($p < 0.001$) than in the normal growth group (2493 ± 651 grams). The fetus's weight will be heavier if it has a higher average gestational age at birth. Fetal growth restriction is 1.97 times more likely to have adverse neonatal outcomes than fetuses with normal growth (OR: 1.97; 95% CI: 1.33 - 2.91). In this study, the average umbilical arterial blood pH of normally growing fetuses (7.26 ± 0.02) was greater than that of restricted growing fetuses (7.22 ± 0.04), and the difference was significant statistically.

The results of this study, which align with current recommendations, underscore the crucial role of the weight percentile cutoff in diagnosing fetal growth restriction. This finding is of significant importance, providing further evidence for the consensus in the field.

4.1.4 Predictive value of umbilical artery pulsatility index, cerebro-placental ratio, umbilico-cerebral ratio for adverse neonatal outcomes

Our study shows that the umbilical pulsatility index has moderate predictive value for adverse perinatal outcomes in fetal growth restriction. Diagnosing adverse neonatal outcomes using the umbilical artery pulsatility index at the cutoff point of 1.08 has a sensitivity of 68.9% and specificity of 73.1%. Nguyen Tran Thao Nguyen and colleagues chose a cutoff point of 1.43 for the umbilical artery pulsatility index to predict adverse neonatal outcomes with a sensitivity of 56.67% and specificity of 89.74%. Yilmaz C.'s study on late-onset growth restriction fetuses with an average gestational age at birth of 37 weeks, with a cutoff point of 1.23 of the umbilical artery pulsatility index, showed results in predicting adverse neonatal outcomes with AUC = 0.853 ($p < 0.001$) and sensitivity 75%, specificity 97.4%.

The results of our study show that the cerebro-placental ratio and the umbilico-cerabral ratio both have low predictive value for adverse perinatal outcomes. Research on growth-restricted fetuses by Coenen H. showed that the predictive ability of the cerebro-placental ratio for umbilical artery blood pH < 7.20 has an AUC of 0.461. Rizzo G.'s prospective study on single fetuses with late-onset growth restriction, the AUC of the cerebro-placental ratio in predicting adverse perinatal outcomes was also low.

4.2 DOPPLER INDICES OF PULMONARY VEINS AND MAIN PULMONARY ARTERY IN FETAL NORMAL GROWTH AND FETAL GROWTH RESTRICTION

4.2.1 Reference value range of pulmonary vein Doppler indices in normally growing fetuses

In this study, peak systolic and diastolic velocities increased significantly from 28 weeks gestation. Peak systolic and diastolic velocities strongly correlate with gestational age. The peak velocity index and pulmonary vein pulsatility index gradually decrease with gestational age, meaning the wave pulsation of flow decreases with pregnancy. The reference value range of pulmonary vein Doppler indices we established is also consistent with the studies of authors Lenz F., Laudy JAM., Dong FQ., Hong Y., Bahlmann F.

4.2.2 Reference value range of main pulmonary artery Doppler indices in normally growing fetuses

In this study, Doppler indices of the main pulmonary artery, such as peak systolic velocity, acceleration time, ejection time, and AT/ET ratio, gradually increased and correlated positively with gestational age. The pulmonary artery pulsatility index has a negative correlation with gestational age. The range of reference values of pulmonary artery Doppler indices is also consistent with the studies of authors Chaoui R., Guan Y., Mielke G., Sosa-Olavarria A., Yamamoto Y.

4.2.3 Characteristics of fetal pulmonary venous pulse index according to fetal growth classification

Our study results showed that the average value of the fetal pulmonary venous pulse index in the group of fetuses with growth restriction (1.13 ± 0.21) was higher than in the group of fetuses with normal growth (0 .85 ± 0.15); this difference is statistically significant with $p < 0.001$. The study of Bravo-Valenzuela et al. also showed that the pulmonary vein pulsatility index in the fetal growth restriction group (1.27 ± 0.39) was higher than the normal growth fetus group (0.75 ± 0.12) with $p < 0.001$.

4.2.4 Characteristics of AT/ET ratio and main pulmonary artery pulsatility index of the fetus according to fetal growth classification

This study showed that the AT/ET ratio in the group of fetuses with growth restriction (0.220 ± 0.032) was statistically significantly lower ($p < 0.001$) than in the group of fetuses with normal growth (0.237 ± 0.024). A study by Sahin also showed a statistically significant difference ($p < 0.001$) between the group of fetuses with normal growth and the group of fetuses small for gestational age, in which the AT/ET ratio of the two groups was 0.348 ± 0.213 and 0.309 ± 0.18, respectively. The average value of the AT/ET ratio in Sahin's study is higher than in our study because Sahin's study sample had a higher gestational age at birth.

Our study shows that the pulmonary artery pulsatility index in the group of fetal growth restriction (2.73 ± 0.26) is higher than the group of fetuses with normal growth (2.60 ± 0.29); the difference is statistically significant. Cynober E.'s research showed that the pulmonary artery pulsatility index in the group of fetuses with growth restriction was 2.71 ± 0.33; this value was higher than that in the group of fetuses with normal growth ($p < 0.01$).

4.3 PREDICTIVE VALUE OF PULMONARY VEIN PULSATILITY INDEX AND FETAL MAIN PULMONARY ARTERY DOPPLER INDEX FOR FETAL AND NEONATAL HEALTH IN FETAL GROWTH RESTRICTION

4.3.1 Predictive value of main pulmonary vein pulsatility index for fetal and neonatal health in fetal growth restriction

In this study, we found a positive correlation between the umbilical artery pulsatility index and the pulmonary vein pulsatility index ($r = 0.59$; $p < 0.0001$) in the group of fetuses with growth restriction. In addition, there was a moderate negative correlation between the pulmonary venous pulse index and the brain-placental ratio in growth-restricted fetuses ($r = -0.34$ and $p < 0.01$). When we searched the literature, we found this was the first study to consider these correlations.

Our study results show a negative correlation between the pulmonary vein pulsatility index and the umbilical artery blood pH with $r = - 0.61$ in growth-restricted fetuses ($p < 0.001$). In 2021, Suekane T. announced a negative correlation ($r = -0.677$) between the ductus venosus pulsatility index and umbilical artery blood pH of fetal growth restriction.

The diagnostic and predictive value of the pulmonary vein pulsatility index of fetal growth restriction for umbilical artery blood pH below 7.20 (table 3.14) has sensitivity: 87.5% (95% CI: 75, 9% - 94.8%), specificity: 70.1% (95% CI: 62.2% - 77.2%, AUC = 0.78 (95% CI: 0.72 – 0.84), positive predictive value: 51.6% (95% CI: 45% - 58%) and negative predictive value: 93.9% (95% CI: 88.5% - 96.8%). Searching the literature, this is the first study to investigate the role of the pulmonary vein pulsatility index in the diagnosis and predict the pH of umbilical artery blood in fetal growth restriction.

Our study's results have practical implications, suggesting that pulmonary vein Doppler should be incorporated into the monitoring of fetal growth restriction. By integrating the pulmonary vein pulsatility index into the pH of the umbilical blood prediction model, which currently includes only gestational age, CTG, and the umbilical artery pulsatility index, we can enhance the accuracy of the results (R2 increasing from 0.569 to 0.615), thereby improving the management of fetal growth restriction in clinical settings.

A prediction model for umbilical artery blood pH < 7.20 in fetal growth restriction has been established based on the results of multivariate regression analysis (table 3.16):

(a) Unstandardized regression equation: UA pH = (-.004) * GA + (-0.026) * CTG + (-0.059) * UAPI + (-0.064) * PVPI + 7.524.

(b) Standardized regression equation: UA pH = (-0.228) * GA + (-0.458) * CTG + (-0.371) * UAPI + (-0.312) * PVPI + 7.524.

(UA: Umbilical Artery; CTG: Cardio Toco Graphy; UAPI: Umbilical Artery Pulsatility Index; PVPI: Pulmonary Vein Pulsatility Index)

The newly established linear regression equation will reveal some additional characteristics of umbilical artery blood pH of growth-restricted fetuses as follows: one week increase in gestational age reduces blood pH by 0.004; If CTG results are suspicious or abnormal, blood pH decreases to 0.026 and 0.052, respectively; The umbilical artery pulsatility index increases by 1 unit, the blood pH decreases by 0.059, the pulmonary vein pulsatility index increases by 1 unit, the blood pH decreases by 0.064. At the same time, the impact level of factors affecting the prediction of umbilical artery blood pH in growth-restricted fetuses is arranged from high to low as follows: CTG results, umbilical artery pulse index, pulmonary vein pulsatility index, and gestational age.

The diagnostic value of adverse neonatal outcomes at the pulmonary vein pulsatility index's cutoff point of 1.09, with a sensitivity of 62.9% and specificity of 83.3%, can be applied in clinical practice because AUC = 0.783 ($p < 0.001$). Interestingly, the difference was not statistically significant ($p > 0.05$) when comparing the diagnostic value of the umbilical artery pulsatility index (AUC = 0.768) with the pulmonary vein pulsatility index (AUC = 0.783) for adverse neonatal outcomes in growth-restricted fetuses. Searching the medical literature, we found that this research direction was newly conducted, and the first results were published.

4.3.2 Predictive value of main pulmonary artery Doppler indices for fetal and neonatal health in fetal growth restriction

Although the changes in the AT/ET ratio and fetal pulmonary artery pulsatility index in the fetal growth restriction group were statistically significant, our study found that these were only hemodynamic fluctuations. The AT/ET ratio can predict umbilical artery blood pH in fetal growth restriction but at a poor level (AUC = 0.620 and p = 0.006). In addition, the pulmonary artery pulsatility index of growth-restricted fetuses had no predictive value for umbilical artery blood pH < 7.20 (AUC = 0.571; p > 0.05). Regarding the ability to search for related publications, this is the first study to examine the relationship between AT/ET ratio, pulmonary artery pulse index, and umbilical artery blood pH.

In our study, the cutoff point of 0.219 of the pulmonary artery’s AT/ET ratio was used to diagnose neonatal respiratory distress in the group of fetuses with growth restriction with a sensitivity of 72.7%; Specificity 85.0%; AUC = 0.849 and p < 0.001. The optimal cutoff point of the AT/ET ratio to diagnose neonatal respiratory distress in our study is lower than in previously published studies. Two main differences lead to this result. First, our study sample’s average gestational age was lower than in previous studies. In addition, previous studies only focused on the predictive value of the AT/ET ratio for respiratory distress syndrome, while respiratory distress syndrome is only one of the causes of respiratory distress in newborns.

To limit errors of the main pulmonary artery's AT/ET cutoff point in predicting neonatal respiratory distress because it depends on the average gestational age of the study sample, we propose to use the percentile classification of the AT/ET ratio to replace the cutoff point. Therefore, our study shows that the AT/ET ratio below the 5th percentile according to gestational age is meaningful in predicting neonatal respiratory distress in growth-restricted fetuses, with a sensitivity of 68.8% (95%CI: 57.2% - 79.9%); specificity of 84.9% (95% CI: 77.7% - 90.6%); AUC: 0.77 (95% CI: 0.70 – 0.82); positive predictive value: 72.6% (95% CI: 63.3% - 80.3%) and negative predictive value: 82.5% (95% CI: 77% - 86.8%) (table 3.18). After searching the literature, this study may be the first to evaluate the role of the AT/ET ratio in predicting respiratory distress in fetal growth restriction. Guan Y.'s publication in 2015 showed that if using the AT/ET ratio classification below the 5th percentile, it would be possible to diagnose neonatal respiratory distress syndrome in normally growing fetuses with a sensitivity of 71.4. % and specificity 93.1%.

CONCLUSION

1. PULMONARY VEIN PULSATILITY INDEX AND PULMONARY ARTERY DOPPLER INDICES IN FETAL APPROPRIATE GROWTH AND FETAL GROWTH RESTRICTION

Reference value ranges for Doppler indices of fetal pulmonary veins and fetal main pulmonary artery have been established for normally growing fetuses with gestational ages from 28 weeks to 40 weeks.

The pulmonary venous pulse index of growth-restricted fetuses is higher than that of fetuses with normal growth ($p < 0.001$).

The pulmonary main artery's AT/ET ratio in fetuses with growth restriction is lower than in fetuses with normal growth ($p < 0.001$).

The pulmonary artery pulsatility index of growth-restricted fetuses was higher than that of fetuses with normal growth ($p < 0.001$).

2. PREDICTIVE VALUE OF PULMONARY VENOUS PULSE INDEX AND PULMONARY ARTERY DOPPLER INDICES FOR FETAL AND NEONATAL HEALTH IN FETAL GROWTH RESTRICTION

2.1 Predictive value of pulmonary vein pulsatility index for fetal and neonatal health in fetal growth restriction

Negative correlation between pulmonary venous pulse index and umbilical artery blood pH in growth-restricted fetuses: $r = -0.61$ ($p < 0.001$).

Diagnostic and prognostic value of pulmonary venous pulse index above the 95th percentile for umbilical artery blood pH < 7.20 in growth-restricted fetuses:

+ Sensitivity: 87.5% (95% CI: 75.9% – 94.8%)
+ Specificity: 70.1% (95% CI: 62.2% - 77.2%)
+ Positive predictive value: 51.6 % (95% CI: 45.0% - 58%)
+ Negative predictive value: 93.9 % (95% CI: 88.5% - 96.8%)

+ AUC: 0.78 (95% CI: 0.72 – 0.84)

Model to predict umbilical artery blood pH < 7.20 in fetal growth restriction:

(a) Unstandardized regression equation: UA pH = (-.004) * GA + (-0.026) * CTG + (-0.059) * UAPI + (-0.064) * PVPI + 7.524.

(b) Standardized regression equation: UA pH = (-0.228) * GA + (-0.458) * CTG + (-0.371) * UAPI + (-0.312) * PVPI + 7.524.

(UA: Umbilical Artery; CTG: Cardio Toco Graphy; UAPI: Umbilical Artery Pulsatility Index; PVPI: Pulmonary Vein Pulsatility Index)

The cutoff point of 1.09 of the pulmonary vein pulsatility index is valuable for diagnosing adverse neonatal outcomes in growth-restricted fetuses with a sensitivity of 62.9% and specificity of 83.3% (AUC = 0.783; p < 0.001).

2.2 Predictive value of the main pulmonary artery Doppler indices for fetal and neonatal health in fetal growth restriction

The pulmonary artery AT/ET ratio of growth-restricted fetuses has little predictive value in umbilical artery blood pH < 7.20.

The pulmonary artery pulsatility index of growth-restricted fetuses has no predictive value in umbilical artery blood pH < 7.20.

The cutoff point of 0.219 of the main pulmonary artery AT/ET ratio is valuable for diagnosing neonatal respiratory distress in fetal growth restriction with a sensitivity of 72.7% and specificity of 85.0% (AUC = 0.849; p < 0.001).

Diagnostic and predictive value of the main pulmonary artery's AT/ET ratio below the 5th percentile for neonatal respiratory distress in fetal growth restriction:

+ Sensitivity: 68.8% (95% CI: 57.2% – 78.9%)

+ Specificity: 84.9% (95% CI: 77.7% - 90.6%)

+ Positive predictive value: 72.6% (95%CI: 63.3% - 80.3%)

+ Negative predictive value: 82.5 % (95% CI: 77.0% - 86.8%)

+ AUC: 0.77 (95% CI: 0.70 – 0.82)

Formula to predict the probability of neonatal respiratory distress in fetal growth restriction:

$$P = \frac{e^{\left(22,637 + (-0,672 \text{ x } AG) + \left(1,979 \text{ x } C\frac{AT}{ET}\right)\right)}}{1+e^{\left(22,637 + (-0,672 \text{ x } AG) + \left(1,979 \text{ x } C\frac{AT}{ET}\right)\right)}}$$

(GA: *Gestational Age*; $C\frac{AT}{ET}$: *Classify the ratio of Acceleration time / Ejection time according to the 5th percentile*)

PROPOSAL

(1) Apply the newly established reference range of Doppler indices of the fetal pulmonary veins and the main pulmonary artery to find Doppler abnormalities in the fetal pulmonary circulatory system.

(2) Coordinate with the pulmonary vein pulsatility index to improve the ability to accurately predict umbilical artery blood pH using a newly established prediction model and predict adverse neonatal outcomes in managing fetal growth restriction.

(3) Survey the AT/ET ratio of the fetal main pulmonary artery to predict the possibility of neonatal respiratory distress using a newly established respiratory failure prediction model.

PUBLICATION OF RESEARCH RESULTS FROM THESIS

A. SCIENTIFIC ARTICLES

1. Phạm Minh Sơn, Nguyễn Vũ Quốc Huy, Trần Đình Vinh (2018), "Tổng quan về xử trí thai chậm tăng trưởng trong tử cung", *Tạp chí Y Dược học – Trường Đại học Y Dược Huế,* 8(6): 184-195. DOI:10.34071/jmp.2018.6.25

2. Phạm Minh Sơn, Trần Đình Vinh, Nguyễn Vũ Quốc Huy (2021), "Nghiên cứu thiết lập khoảng giá trị tham chiếu cho các chỉ số Doppler tĩnh mạch phổi ở thai nhi có tăng trưởng bình thường", *Tạp chí Y Dược học – Trường Đại học Y Dược Huế*, 11(3): 86-93. DOI:10.34071/jmp.2021.3.12

3. Phạm Minh Sơn, Trần Đình Vinh, Nguyễn Vũ Quốc Huy (2021), "Nghiên cứu thiết lập khoảng giá trị tham chiếu cho các chỉ số Doppler động mạch phổi ở thai nhi có tăng trưởng bình thường", *Tạp chí Phụ sản*, 19(1): 16-22. DOI:10.46755/vjog. 2021.1.1177

4. Minh Son Pham, Dinh Vinh Tran, Chi Kong Pham, Thi Linh Giang Truong, Vu Quoc Huy Nguyen (2023). "Added value of the pulmonary vein pulsatility index and its correlation to neonatal umbilical artery pH in fetal growth restrictions: a Vietnamese matched cohort study", *BMC Pregnancy and Childbirth* 23, 625. https://doi.org/10.1186/s12884-023-05910-0.

B. REPORTS AT CONFERENCES

5. M. Pham, D. Tran, V. Nguyen (2023), *"Predictive value of the fetal pulmonary artery Doppler echocardiography for neonatal respiratory distress in pregnancy with fetal growth restriction"*, Int J Gyn Obstet*,* Special Issue: Abstracts of the XXIV FIGO World Congress of Gynecology & Obstetrics, 163(Suppl. 1), 480 -481

6. Phạm Minh Sơn, Trần Đình Vinh, Nguyễn Vũ Quốc Huy (2018), *"Tổng quan về chẩn đoán và quản lý thai chậm tăng trưởng theo các khuyến cáo cập nhật"*, Báo cáo tại Hội nghị Khoa học sau đại học 2018 – Trường Đại học Y Dược Huế, Thành phố Huế, tháng 12.

7. Phạm Minh Sơn, Trần Đình Vinh, Nguyễn Vũ Quốc Huy (2021), *"Thiết lập khoảng tham chiếu cho các chỉ số Doppler của hệ tuần hoàn phổi thai nhi và tiềm năng ứng dụng vào thực hành lâm sàng trong tương lai"*, Báo cáo tại Hội nghị Phụ sản Miền Trung Tây Nguyên mở rộng lần thứ IX, Thừa Thiên Huế, tháng 10.

8. Phạm Minh Sơn, Trần Đình Vinh, Nguyễn Vũ Quốc Huy (2022), *"Nghiên cứu giá trị của chỉ số xung tĩnh mạch phổi trong tiên lượng pH máu động mạch rốn ở thai chậm tăng trưởng"*, Báo cáo tại Hội nghị Sau Đại học – Nghiên cứu sinh quốc tế lần thứ VI, Thành phố Huế, tháng 07.

9. Phạm Minh Sơn, Trần Đình Vinh, Nguyễn Vũ Quốc Huy (2023), *"Vai trò dự báo của hệ tuần hoàn phổi thai nhi đối với một số kết cục thai kỳ ở thai hạn chế tăng trưởng",* Báo cáo tại Hội nghị siêu âm toàn quốc lần thứ V, Thành phố Huế, tháng 02.

10. Phạm Minh Sơn, Trần Đình Vinh, Nguyễn Vũ Quốc Huy (2024), *"Dự báo pH máu động mạch rốn của thai hạn chế tăng trưởng bằng siêu âm Doppler và CTG"*, Báo cáo tại Hội nghị siêu âm toàn quốc lần thứ VI, Thành phố Huế, tháng 03.