A Clinical Prediction Model to Estimate the Risk for Coarctation of the Aorta: From Fetal to Newborn Life

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Research Article

Keywords: prenatal diagnosis, coarctation of the aorta, prediction model, logistic regression

Posted Date: August 4th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-724289/v1>

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Abstract

Purpose: This study aimed to develop a coarctation probability model incorporating prenatal cardiac sonographic markers to estimate the probability of an antenatal diagnosis of coarctation of the aorta (CoA).

Methods: We reviewed 89 fetuses as a “investigation” cohort with prenatal suspicion for CoA and allotted to three subgroups: (1) severe CoA: symptoms onset of CoA and surgery within the first three months (15); (2) mild CoA: surgery within four months-one year (29); (3) false-positive CoA: this outcome does not require surgery (45). Using logistic regression to create the multi-parametric model, and validated using a “validation” cohort of 86 fetuses with suspected CoA subsequently.

Results: The prediction model had optimal criterion >0.25 with sensitivity 97.7% and specificity 59.1%, the area under the receiver operator curve is 0.8 which makes sense in diagnosis of CoA and risk stratification. The risk assessment demonstrated that fetuses with model probability $>60\%$ should make an inpatient observation for high risk of CoA whereas $<15\%$ should not undergo clinical follow-up imaging.

Conclusion: Based on these results, we recommend measuring the model in all fetuses with suspected CoA may improve the accuracy of risk assessment. The objectivity of its parameters may allow its implementation working in multicenter studies of fetal cardiology.

Introduction

The diagnosis of Coarctation of the aorta (CoA) prenatally is one of the difficult and key items for sonographers. The catheter organization theory states that the narrowing of the aorta is due to the displacement of smooth muscle cells growing in the aorta[1], and the hemodynamic theory states that the narrowing of the aorta is due to the decrease in blood flow through the aortic arch during the fetal period[2], which is responsible for false negative and false positive diagnoses at fetal echocardiography. Severe constriction to flow through the descending aorta will not occur antenatally due to ductal patency, which lead to potentially lethal consequences as the patent ductus arteriosus (PDA) closes spontaneously in postnatal life[4]; therefore, how to avoid abortion due to overdiagnosis and postnatal deaths due to omission? The diagnosis relies on more indirect signs in fetuses with ventricular asymmetry. Multiple criteria-prediction diagnostic models integrating different ultrasound signs replaced isolated parameters for the detection of CoA have been increased, especially fetal echocardiographic scoring models have been suggested[3, 12, 13]. This study primarily aimed to confirm the parameters associated with the diagnostic accuracy of CoA and create a non-invasive model to help rule out or screen out CoA in an equivocal fetus. The secondary aim was to predict the probability of CoA, helping clinicians in risk profiling and decision making in patients with unconfirmed CoA.

Material And Methods

Fetal Echocardiography and Perinatal Management of the Investigation Cohort

We reviewed fetuses with prenatal suspicion for CoA as a “investigation” cohort. This retrospective study was conducted which included all fetuses from the Shandong Provincial Hospital Central Campus and Shandong Maternity and Child Care Hospital database between May 2015 and May 2020 with available follow-up data postnatally. This study was performed at a tertiary first-class hospital. All fetuses and neonates with CoA were included in the investigation cohort. Institutional review board approval was obtained for this study, and the need for patient consent was waived. Exclusion criteria included pregnancy termination, fetal death in utero, difficulty in obtaining clear images, unavailable postnatal follow-up data, and incorporated with other major extracardiac abnormalities. Based on their postnatal outcomes, the fetuses were divided into the following groups: the true-positive group, which included those fetuses who subsequently required arch surgical repair, according to the operation time, the patients were divided into a severe group ($n = 15$) and a mild group ($n = 29$); and a false-positive group, which included those fetuses who were subsequently did not require aortic arch surgery ($n = 45$) (Fig. 1). To analyze the morphological differences of the aorta between the groups, 51 cases of the control group were included (Table 2). Fetal echocardiography was performed using a Philips IE33 or GE Vivid E9 ultrasound machine.

Combining appropriate software used to calculate the Z-score for most heart sizes[7, 11]. Characteristic of the investigation cohort were measured in Table 1. From the sagittal aortic arch view during systole, we obtained the transverse arch diameter (DT), and distances between the left subclavian artery (LSCA) and the common carotid artery (LCCA)(Fig. 2a) [8–11]. Measuring method of (AAo-DAo) angle and (TAo-DAo) are introduced in Fig. 2b and Fig. 2c. All measurements were performed retrospectively and blinded by reviewers(W,HH.and F.J.) to the outcomes by experienced investigators (Z.M. and L.H.) confirming CoA. A single investigator (S.A.) reviewed all measurements from the archived records.

Table 1
Charateristic of the investigation cohort

Charateristic	Group			P Value	F
	Severe CoA N = 15	Mild CoA N = 29	False positive CoA N = 45		
GA at first echo Median(range)	29.33 ± 3.9	28.5 ± 3.5	29 ± 3.7	0.746	0.294
≤ 28wk(%)	7(47)	14(48)	21(26)		
> 28wk(%)	8(53)	15(52)	34(74)		
GA at birth	38 ± 1.4	38.5 ± 0.99	38 ± 1.3	0.627	0.469
Gender F(%)	7(47)	13(45)	21(46)		
M(%)	8(53)	16(55)	24(53)		
Mean AAO peak Doppler Z-score Z-score	-0.66 ± 1.33 *	-1.4 ± 0.89	-1.6 ± 0.95*	0.042	3.050
AAo Z-score	-0.34 ± 0.44*	-0.18 ± 0.61	0.15 ± 1.15*	0.065	2.817
MPA Z-score	2.47 ± 0.85	2.41 ± 1.10	2.31 ± 1.12	0.477	0.747
Mean RVEDD Z-score	0.26 ± 1.5	0.24 ± 1.5	-0.85 ± 2.0	0.520	0.658
Mean LVEDD Z -score	-3.89 ± 1.46	-2.7 ± 1.5	-2.5 ± 1.9	0.965	0.035
Mean RVEDD/ LVEDD	1.67 ± 0.54*	1.46 ± 0.52	1.34 ± 0.26*	0.003	6.403
Aortic Isthmus Z-score	-4.68 ± 2.12*	-2.95 ± 2.39	-2.43 ± 2.49*	0.412	0.897
VSD(%)	7(47)	14(48)	11(24.4)	0.07	
LSVC(%)	4(27)	6(20.7)	7(15.5)	0.584 ^a	
BAV(%)	3(20)	3(10.33)	2(4.4)	0.12 ^a	
PFO restricted shunt(%)	5(33.3)	4(13.79)	12(26.66)	0.296 ^a	
Data is described as mean ± standard deviation unless otherwise stated. *Statistical significance was set at a p < 0.05					
^a Fisher's Exact test for all pair-wise differences are not significant at alpha = 0.017					

Charateristic	Group			P Value	F
	Severe CoA N = 15	Mild CoA N = 29	False positive CoA N = 45		
AoI-R %	5(33.3)	5(17.24)	7(15.55)	0.41 ^a	
Data is described as mean ± standard deviation unless otherwise stated. *Statistical significance was set at a p < 0.05					
^a Fisher's Exact test for all pair-wise differences are not significant at alpha = 0.017					

Postnatal echocardiography was implemented using Phillips IE33, Phillips CX50, or GE Vivid E9 device. The first echocardiogram was examinationed for the presence or absence of CoA within 24h of birth. The diagnosis of CoA relies on the presence of localized narrowing of the descending aorta just beyond the origin of the LSCA together with high flow velocity (> 2 m/s) complicated with loss of pulsatility of the abdominal aorta[16],the presence or absence of VSD,bicuspid aortic valve (BAV), left superior vena cava (LSVC), and PDA were also noted. The decision to start prostaglandin E2 after birth was decided at the last assessment and was reviewed following the initial postnatal echocardiography. In inconclusive cases or when a PDA precludes confirmation or exclusion of CoA, clinical monitoring and following echocardiographs are performed until such a diagnosis can be established and then grouped according to the operation time.

Fetal Echocardiography and Perinatal Management of the Validation Cohort

We prospectively collected 136 fetuses from the Shandong Provincial Hospital East Campus and Jinan Maternity and child care Hospital with suspected CoA over two years (November 2018 to November 2020), and enrolled in this study for training for validation cohort. The screening criteria were equivalent to those of the investigation cohort. During that time, 86 fetuses met the inclusion criteria(Fig. 1); Clinical decision was not maked towards the model. By the end of two-years, demographic data and arch measurements for all fetuses and their end in the validation cohort were collected.

Statistical Analysis

Continuous variables were compared between groups using the unpaired t-test. The t-test or analysis of variance was used for normal distribution, non-normal distribution using Mann-Whitney U test. Categorical variables were compared using the Pearson χ^2 test or Fisher's exact test. Statistical significance was established at $\alpha = 0.017$, Bonferroni correction used for three between-group comparisons. Univariate analysis was performed to assess the factors associated with coarctation. We fited an equation for our model used logistic regression analyses to estimate the probability of CoA, which characterized the discriminative parameters to assess their interdependence and to select the best combination. The receiver operating characteristic (ROC) curve was used to analyze the specificity and

sensitivity of the discriminative parameters. The model was internally validated and calibrated using bootstrapping(Fig. 3c). All analyses were performed using the SPSS Statistics for Windows. R version 4.0.5 (Shake and Throw) was used to generate a nomogram for binary logistic regression predictive models. The level of statistical significance was set at $P < 0.05$.

Results

Of the 148 fetuses in the investigation cohort, 59 fetuses were excluded, 13 fetuses for inadequate fetal imaging, 15 fetuses for insufficient postnatal follow-up data, 3 fetuses due to death in utero, 5 fetuses due to postnatal death, fetal karyotyping was performed in 80 cases, 23 fetuses due to miscarriage (2 miscarriages due to trisomy 18, 3 miscarriages due to trisomy 21, 1 miscarriage due to urinary malformation, 3 miscarriages due to nervous system malformations). A total of 89 neonates with prenatal suspicion of CoA were eventually included in the study. Of the 89 fetuses in the investigation cohort, 15 had CoA and underwent surgery within three months of birth (median 52 days), and the remaining 74 newborns were closely observed until the PDA was closed until the end of the follow-up. 29 newborns with suspected CoA underwent aortic arch surgery within three months to a year after birth (mild group); 45 (50.6%) newborns did not require aortic arch intervention (false-positive group), 11 of whom only underwent VSD repair surgery, as depicted in Table 1. None of the controls had any additional defects.

There was a difference observed between Mean right ventricle end-diastolic dimensions (RVEDD) and left ventricle end-diastolic dimensions (LVEDD) ($P = 0.003$). The severe group had significantly lower Z scores for the ascending aorta peak velocity(Z-VAo), aortic isthmus, and ascending aorta between false positives ($P = 0.04$). Measurement of Gestational Age(GA), main pulmonary artery (MPA) Z-score, retrograde blood flow in the aortic isthmus(AoI-R), BAV, patent foramen ovale (PFO) restricted shunt, and LSVC did not distinguish between true and false-positive fetuses. However, the above categorical variables were observed more frequently in the severe group than in the other groups(Table 1).The indices of LCCA-LSCA/DT, AAO-DAo angle and TAO-DAo angle were compared between 52 control fetuses and investigation cohort (Table 2). Among the control subjects, the LCCA-LSCA/DT diameter ratio and AAO-DAo angle were statistically significant in predicting CoA compared with the three study groups; the severe group demonstrated a higher LCCA-LSCA/DT diameter ratio towards the false-positive CoA group ($P = 0.001$). The difference in the TAO-DAo angle and TAO-DAo/AAO-DAo angle ratio between the four groups were not statistically significant ($P > 0.05$). Intraclass correlation coefficients (ICC)for all variables ranged from 0.7 to 0.9 in this investigation cohort.

Table 2
Investigation cohort aortic arch findings

Variable	False positive CoA N = 45	Mild CoA N = 29	Severe CoA N = 15	Normal N = 52	P Value	F
AAO-DAO/TAO-DAO angle ratio	0.33 ± 0.17	0.38 ± 0.42	0.39 ± 0.16	0.19 ± 0.05	.089	2.51
LCCA-LSCA/DT diameter ratio	1.31 ± 0.47* [#]	1.44 ± 0.79 *	2.12 ± 0.86*	1.02 ± 0.81 [#]	.001	15.06
AAO-DAO angle	31.04 ± 15.09*	34.33 ± 19.07*	39.09 ± 14.87*	19.11 ± 3.02	.001	20.83
TAO-DAO angle	95.52 ± 16.98	100.79 ± 21.81	100.59 ± 11.73	94.05 ± 7.96	.052	2.54
* [#] Statistical significance was set at a p < 0.05.						

Individual Indices Modeling and Validation

The model was created using the investigation cohort. The equation is

$$P = \frac{1}{1 + \exp[-2.05 + 1.879 * (LCCA - LSCA) / DT - 1.51 * VSD + 0.67 * (ZVAo)]}$$

Among the three predictors, higher LCCA-LSCA/DT (OR = 6.5, CI: 2.4–17.5) and Z-VAo (OR = 1.9, CI: 1.3–3.0) were related to increased risk for CoA. Surprisingly, VSD was identified as a protective factor with OR value is 0.2. The model has good predictability for CoA (AUROC = 0.85) (Fig. 3a). Among all variables studied, the LCCA-LSCA/DT diameter ratio had the highest sensitivity (62%) and specificity (88%) for detecting CoA. Bootstrapping was used to validated and calibrated the model internally, Fig. 3c depicts the calibration curve of the model, which predicted and observed data fitting effect. The plot demonstrates good calibration and minimal over fitting. Cut-off values for these variables yielding the best prediction, sensitivity and specificity, and the $\pm$ LRs calculated obtained are shown in Table 3. A multivariable threshold scoring system identified fetuses with CoA with greater sensitivity (98%) and decreased specificity (59%).

Table 3

Predictive value of echocardiographic thresholds for detection of confirmed fetal coarctation of the aorta

Variable	Criterion	Sensitivity	Specificity	+PV	-PV
LCCA-LSCA/DT Index	> 1.33	80(65.4–90.4)	50(34.6–65.4)	62.1(54.1–69.5)	71(55.9–82.5)
AUROC: 0.76	> 1.77	62.22(46.5–76.2)	88.64(75.4–96.2)	84.8(70.4–92.9)	69.6(60.8–77.2)
criterion 1.77	> 2.11	42.22(27.7–57.8)	93.18(81.3–98.6)	86.4(66.8–95.2)	61.2(54.8–67.2)
(95% CI: 0.658 – 0.858)					
AAO-DAO angle	> 16.5	97.78(88.2–99.9)	13.64(5.2–27.4)	53.7(50.5–56.8)	85.7(42.9–98.0)
AUROC:0.64	> 22.1	86.67(73.2–94.9)	38.64(24.4–54.5)	59.1(52.7–65.2)	73.9(55.2–86.7)
criterion 31.8°	> 38	42.22(27.7–57.8)	70.45(54.8–83.2)	59.4(45.2–72.1)	54.4(46.5–62.0)
(95%CI: 0.528–0.759)					
TAO-DAO angle	> 92.2	80(65.4–90.4)	50(34.6–65.4)	62.1(54.1–69.5)	71(55.9–82.5)
AUROC: 0.65	> 94.5	75.56(60.5–87.1)	56.82(41.0–71.7)	64.2(55.1–72.3)	69.4(56.1–80.1)
criterion 94.5°	> 100.4	53.33(37.9–68.3)	65.91(50.1–79.5)	61.5(49.4–72.4)	58(48.6–66.8)
(95% CI 0.544–0.751)					
AAo peak Doppler Z-score	>-2.11	91.11(78.8–97.5)	40.91(26.3–56.8)	61.2(54.8–67.2)	81.8(62.3–92.4)
AUROC: 0.71	>-1.7	77.78(62.9–88.8)	56.82(41.0–71.7)	64.8(55.9–72.8)	71.4(57.7–82.1)
criterion >-1.7	>-1.49	66.67(51.0–80.0)	59.09(43.2–73.7)	62.5(52.5–71.5)	63.4(51.7–73.7)
(95% CI 0.606–0.803)					
AUROC: area under receiver operating characteristics curve, +PV: positive predictive value, -PV: negative predictive value, Percentages (95th confidence intervals) are reported for + PV, -PV, sensitivity and specificity CI: confidence interval					

Discussion

To the best of our knowledge, our model is the first risk-prediction nomogram for evaluating the risk of CoA in a fetus. In the present collaborative study, the diagnosis of CoA is possible and is best facilitated by the observation of quantitative distal aortic arch hypoplasia[3, 5, 16]. Morphological characteristics of aortic arch indices such as the LCCA and LSCA diameter of the DT arch, which have already applied to postnatal echocardiograms[6,14 ~ 16]. Our study examined fetal echocardiographic arches and applied these characteristics as the indicators to identify CoA prenatally. Compared with postnatal

echocardiography, fetal aortic arch added benefit of permitting simultaneous visualization perspective of AAO-TAo and AAO-DAo angles.

Among the true-positive coarctation fetuses, a surprising finding was that neither narrow measurement at the isthmus, nor retrograde blood flow of isthmus (AoI-R) was seen more often; in addition, bidirectional flow were observed in a fair number of fetuses who did not develop coarctation postnatally. The LSVC, ventricular size disproportion, and PFO restricted shunt did not help in diagnosing true coarctation. VSD was more common in the true-positive group, whereas it is interesting to note that VSD is a protective factor for CoA; however, in the nomogram analysis, the presence of VSD still increases the risk of CoA, which cannot be considered a failed study. In other words, in fetuses with VSD, CoA should be diagnosed more cautiously. The velocity of the descending aorta after VSD repair postnatally may be acceptable in the short term.

The measurement of the morphology of the aortic arch showed a very clear pattern at the very least we can say, as the ratio of LCCA-LSCA/DT increases, the degree of constriction also increases. We suggest that a higher LCCA-LSCA/DT(> 1.7) can be used as an indicator of coarctation throughout pregnancy; the higher the ratio, the higher the specificity of the diagnosis; however, it results in reduced sensitivity to constriction. The same conclusion applies to a higher Z-VAo, which leads to low flow resulting in abnormal narrow growth of the vessels of the aortic arch, which is not surprisingly a common subject in fetal cardiology[18]. Although the angle of the aortic arch was not included in the model, compared with the normal group, the AAO-DAo angle is still meaningfully distinguished in the true-positive group from the false-positive group. The angle between AAO-DAo and TAo-DAo in the diseased group was more obtuse, which is different from the results of the study by Bhawna et al[4]. (Table 2).

We analyzed of the Spearman correlation coefficient between LCCA-LSCA/DT and AAO-DAo/ TAo-DAo and found that there was a weak negative correlation between the two in the normal group(Fig. 4). As the degree of constriction increased, the two parameters showed an improved positive correlation; that is, as the distance between LCCA-LSCA increased, the morphology of the entire arch tended to be more obtuse. We theorize that during the early embryological development of the aorta arch with coarctation begins, the course of insertion of the descending aorta into the proximal descending aorta leading to the consequences of losing its original soft shape and replaced by isthmus collapsed relatively, which demonstrated the anatomy of the descending aorta itself have do factor into the occurrence of CoA, especially illustrated the impact on affecting the shape of the arch potentially. Our opinion is identical with Benjamin who demonstrated that the AAO-DAo angle was more acute in fetuses with CoA[19]. This also explains that the ratio of AAO-DAo/TAo-DAo angles in the real CoA group was greater than that in the false-positive group in this study.

Although more experienced echocardiographers had higher accuracy in diagnosing CoA, the measurement of the aortic arch recorded by the echocardiographers correlated well. The measurements of aortic arch parameters used to calculate the prediction model in the validation cohort were performed prospectively without remeasure or confirm these data, which make it more intuitive and accurately improve the overall

clinical workflow. By entering the three individual components, namely the LCCA-LSCA/DT, Z-VAo, and VSD into a digital picture archiving or using Fig. 3b, the probabilities can be calculated against the indices data constitute of our model. The calibration accuracy of our original model was perfect through internal calibration. It is almost the same as external validation, which performs good fitting degrees with very low actual prediction probabilities, perhaps ultrasonographers and obstetricians could help in improving fetal echocardiography and avoid high abortion rates (Fig. 3d).

Figure 5 demonstrates the risk stratification of CoA for fetuses among both all groups. As we can see from this output that no fetuses with model probability < 15% had CoA, meanwhile, 58 fetuses with probability > 60% in addition. There was one fetus from investigation cohort and in the mild group with PFO restricted shunts, whose aortic arch was thought unobstructed with a PDA after postpartum echocardiography carried out; however, this patient returned to our hospital due to heart failure six months after birth and have a surprising finding of CoA. After immediately surgical repair, her left ventricular ejection fraction returned to normal within a month. The antenatal echocardiogram of this patient was analyzed in the investigation cohort with model estimated a 46% probability of CoA. Although it belongs to the moderate-risk category, we recommend that fetuses with probabilities above 15% should undergo follow-up imaging scheduled until PDA closure [20].

As in our previous study [21], women pregnant with fetuses suspected to have CoA presented heightened levels of anxiety and depression compared with women pregnant with fetuses having serious heart disease. Our model can provide more effective counseling for pregnant women who are shocked and scared, thereby helping them be better prepared for their delivery.

Conclusions

The model possess high accuracy and can be applied to antenatal diagnosis of CoA simply and efficiently. We recommend, fetus with model probabilities < 15% no need to observed hospitalized, while fetus with model probabilities > 60% need inpatient observation until PDA closure, we suggested the time frame is seven years. The fetal ultrasound parameters of (LCCA-LSCA)/DT, (AAo-DAo) angle and (TAo-DAo) angle may allow its implementation work in fetal cardiology research centre.

Abbreviations

CoA = coarctation of the aorta

LCCA = left common carotid artery

LSCA = left subclavian artery

AAO = ascending aorta

DAO = descending aorta

TAO = transverse aorta

LCCA-LSCA/DT = Left Common Carotid Artery to Left Subclavian Artery distance/Distal Transverse Arch

VSD = ventricular septal defect

Declarations

Funding

The authors gratefully acknowledge the generous support from Key Research and Development Program of Shandong Provincial(2018GSF118112).

Availability of data and material

Data that support the findings of this study have been deposited in <https://doi.org/10.5061/dryad.vdncjsxvf>.

Authors' contributions

All measurements were collection retrospectively and blinded by reviewers(W,HH,F.J and Z,N) to the outcomes by experienced investigators (Z.M, L.H and W,YM) confirming CoA. W,XM is assigned as corresponding author edited this manuscript and as advisor of W,HH. Neonatal monitoring and surgery were carried out by W.AB and Y.YH.

Ethics approval

The local ethics committee approved the study protocol (2017458,from 29 September 2017) and all participants gave written informed consent to participate in this study.

Consent to participate

This study was approved by the ethical committee of Medical Ethics Committee of Shandong Provincial Hospital, and all participants provided informed verbal consent. We obtained the consent of the patient or his immediate family members and the ethics committee approved this procedure.

Acknowledgments

We wish to thank all of the centers and doctors for their hard work and dedication in this collaborative research; and thanks to Liu Zhe,MD.CS kindly provided statistical advice for this manuscript.

Supplementary Information

Data that support the findings of this study have been deposited in <https://doi.org/10.5061/dryad.vdncjsxvf>.

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Figures

Figure 1

Investigation cohort: retrospective review of 89 fetus and neonates who met the inclusion criteria. Neonates with unconfirmed arch diagnoses who required observation in the NICU, of whom 44 had CoA and 45 had unobstructed aortic arches. Validation cohort: 136 met the inclusion criteria, but only 86 had all measurements performed. Of those 86, 30 neonates had CoA and 56 had unobstructed aortic arches.

Figure 2

(a) distal transverse arch diameter(between LCCA and LSCA); DT transverse arch diameter; (b) (AAo-DAo) angle : defined as the angle between two straight lines: along the internal boundary, a straight line from the proximal to the distal in the AAo; and the second line was drawn distal (distal thoracic aorta) to proximal(just prior to the isthmus) of the DAo. (c) (TAo-DAo) angle : formed by two straight lines: a straight line was drawn from the proximal (from the first head vessel) to the distal (to the third head vessel) of aortic arch and the second line was drawn along the DAo as described in the preceding text.

(a)

(b)

(c)

(d)

Figure 3

(a) The area under the receiver operating characteristic curve (AUC) for the model was 0.85. (b). The nomogram allows the calculation of coarctation probability using the logistic regression model. Calculate the LCCA-LSCA/DT, VSD, and Z value of VAo indices, find the point values for each of these indices in the nomogram, drawing a vertical line from the values measured for each index to the “points” scale at the top of the nomogram. Add up the points for all three indices to obtain the total points for that patient. Find the total number of points on the “total points” scale, then draw a vertical line down to the “risk of coarctation” scale to find the predicted probability of CoA. (c). Results of internal validation for the model. (d). External calibration using the validation cohort shows the actual versus predicted probabilities using loess smooth function with 95% bootstrap confidence interval (CI).

Figure 4

Scatter plot and Spearman correlation test between the AAO-DAO/TAO-DAO angle ratio and LCCA-LSCA/DT diameter ratio

Figure 5

Risk stratification using the model. Fetus with probabilities $< 15\%$ were assigned to the category of low risk for CoA, those with probabilities of 15% to 60% to the moderate-risk category, and those with probabilities $> 60\%$ to the high-risk category.