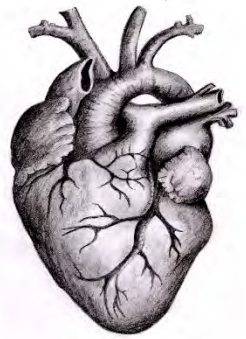
Seattle Children's
HOSPITAL • RESEARCH • FOUNDATION

Validation of Prenatal Aortic Arch Measurements in the Diagnosis of Neonatal Coarctation of the Aorta

Kaitlyn Freeman, DO
Pediatric Cardiology Fellow

Co-authors: Michele Clouse RDCS, Richard Kronmal PhD, Jeffrey Conwell MD, Luciana Young MD, Mark Lewin MD, Bhawna Arya MD



Conflict of Interest Disclosure

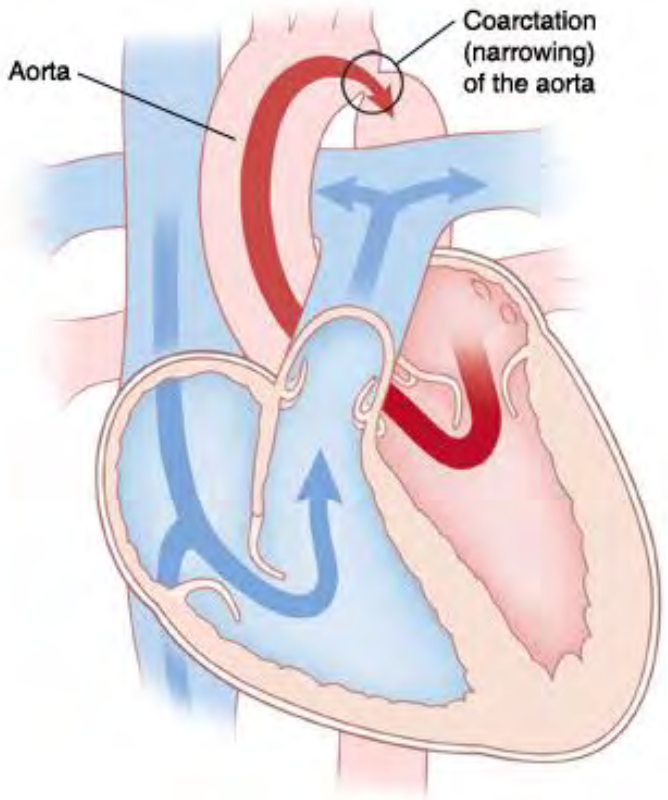
- I have no financial or non-financial relationships to disclose

Background

Coarctation of the Aorta

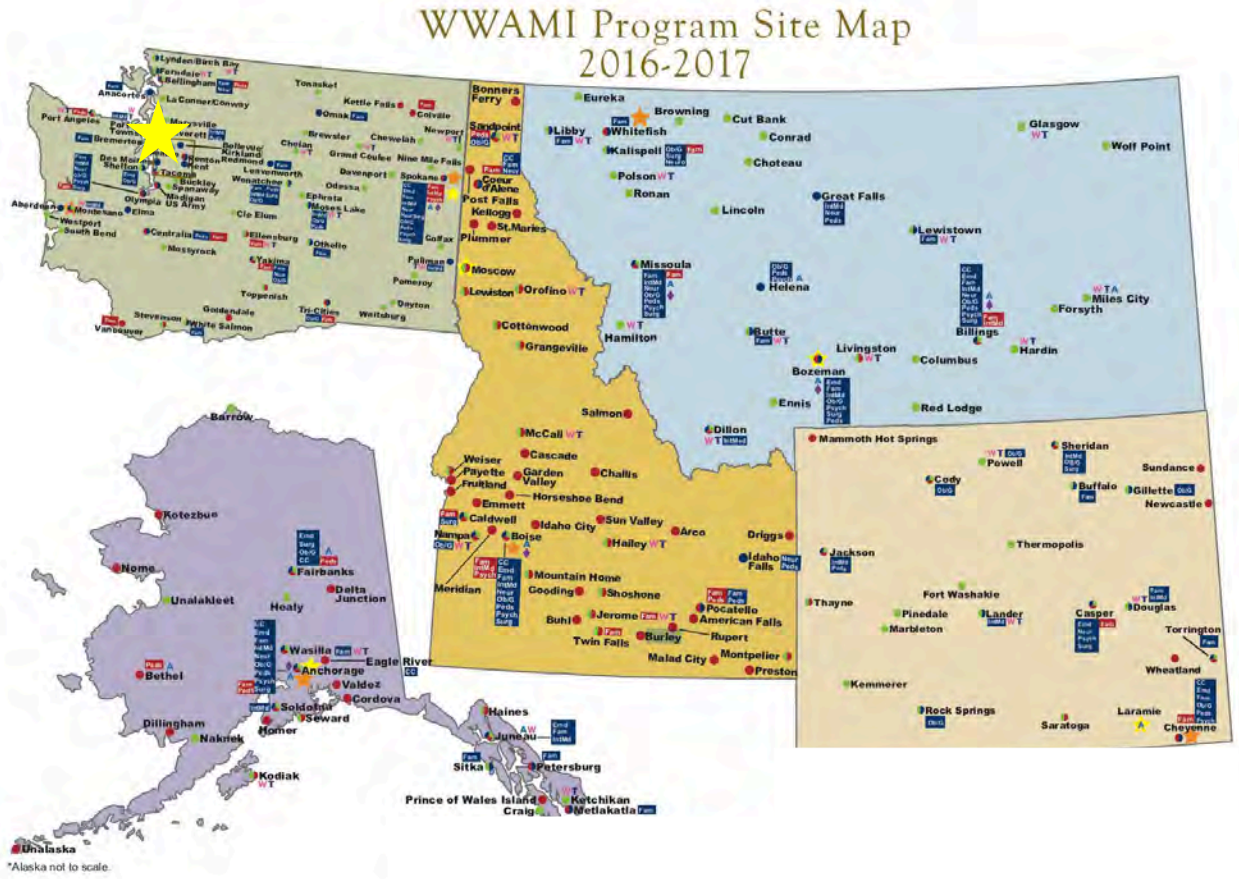
- 60-80% of babies present postnatally due to failure of detection during routine anatomy scans

- Even with prenatal cardiology evaluation there is a very high false positive rate of up to 40%



Familiari, A. et al. Circulation. 2017

Background



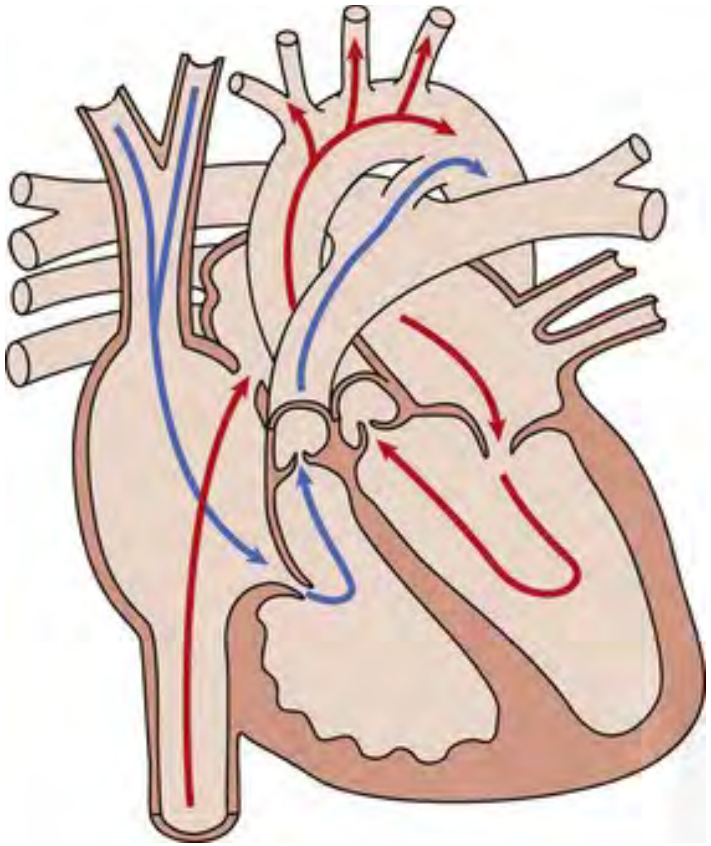
Seattle Children's
HOSPITAL • RESEARCH • FOUNDATION

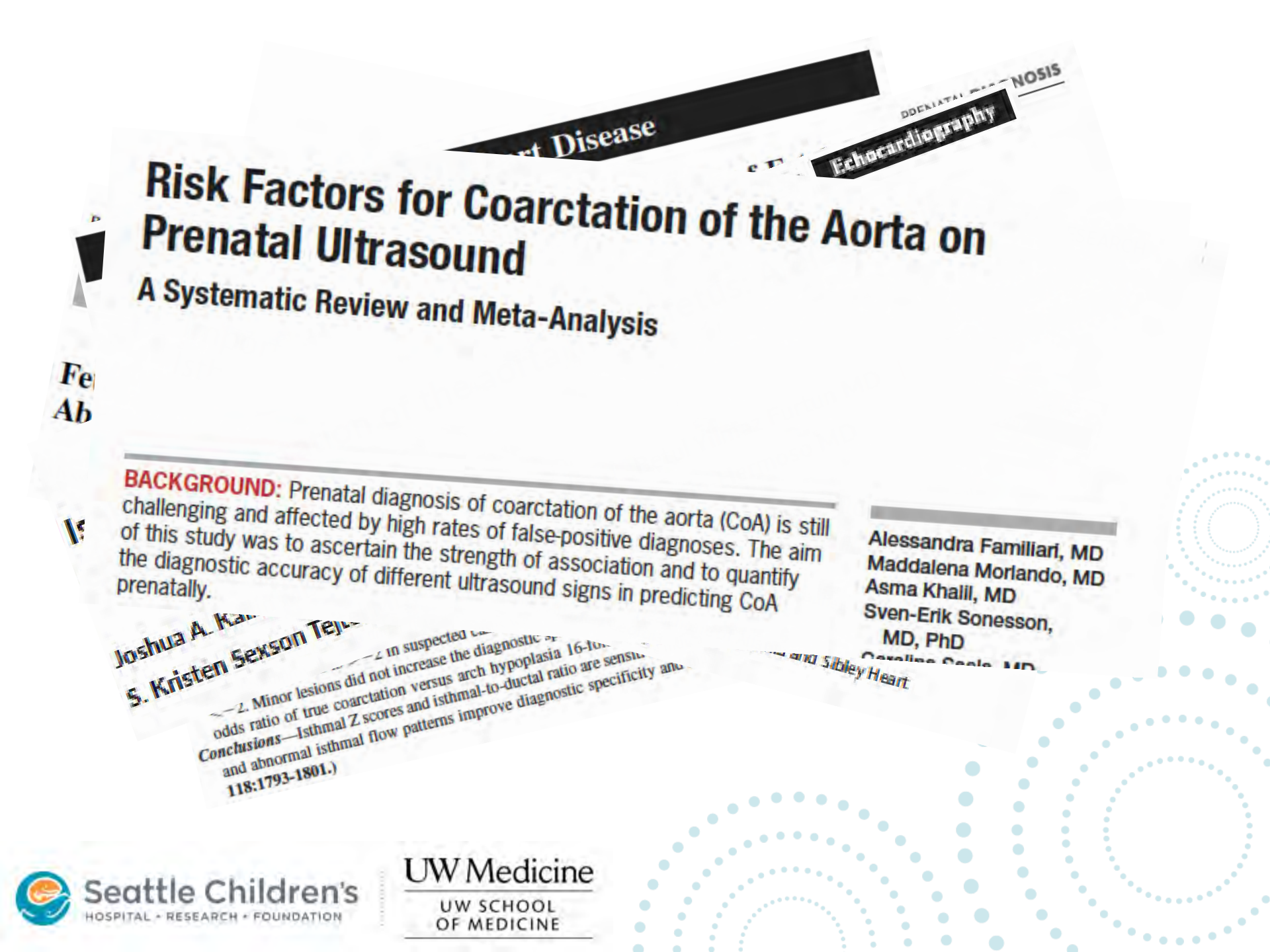
UW Medicine
UW SCHOOL OF MEDICINE

Background

- Prenatal diagnosis of coarctation of the aorta (CoA) is challenging in utero

- Fetal circulation inhibits accurate prenatal diagnosis due to the presence of the ductus arteriosus and the intricacies of fetal circulation





Seattle Children's
HOSPITAL • RESEARCH • FOUNDATION

UW Medicine
UW SCHOOL OF MEDICINE

Background

Table 5. Predictive Models for Coarctation of the Aorta Integrating Multiple Risk Factors

Author	Year	Predictive model	AUC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Arya [14]	2016	AAo-DAo angle+ IAo-DAo angle	NS	95 (75–100)	100 (83–100)
Toole[15]	2015	MV d+MV/TV ratio+ IDD+IDA+IDD	0.92 (0.80–1.00)	85 (66–96)	60 (42–76)
Märginean[16]	2015	RV/LV<1.5+AoI <4.2 mm + AD/AoI >1.4	NS	56 (21–86)	87 (66–97)
Gomez-Montes[19]	2014	*z* score AAo + *z* score AoI (sagittal view) (≤28 wk)	0.88 (0.72–1.00)	60 (41–77)*	78 (45–94)†
Gomez-Montes[19]	2014	*z* score AAo + *z* score AoI (3VT view) (≤28 wk)	0.98 (0.94–1.00)	91 (76–97)*	91 (62–98)†
Gomez-Montes[19]	2014	*z* score AAo + TV/MV ratio (≤28 wk)	0.85 (0.71–0.99)	44 (29–59)*	69 (42–87)†
Gomez-Montes [19]	2014	*z* score AAo + MPA/AAo ratio (≤28 wk)	0.87 (0.76–0.99)	78 (63–88)*	62 (36–82)†
Gomez-Montes[19]	2014	*z* score AoI (sagittal view) + *z* score AoI (3VT view) (≤28 wk)	0.97 (0.91–1.00)	86 (65–95)*	89 (57–98)†
Gomez-Montes[19]	2014	*z* score AoI (sagittal view) + TV/MV ratio (≤28 wk)	0.82 (0.63–1.00)	23 (11–42)*	70 (40–89)†
Gomez-Montes [19]	2014	*z* score AoI (sagittal view) + MPA/AAo ratio (≤28 wk)	0.85 (0.72–0.98)	68 (48–83)*	44 (19–73)†
Gomez-Montes[19]	2014	*z* score AoI (3VT view) + TV/MV ratio (≤28 wk)	0.94 (0.84–1.00)	87 (71–95)*	83 (55–95)†
Gomez-Montes[19]	2014	*z* score AoI (3VT view) + MPA/AAo ratio (≤28 wk)	0.89 (0.75–1.00)	48 (32–65)*	82 (52–95)†
Gomez-Montes[19]	2014	TV/MV ratio + MPA/AAo ratio (≤28 wk)	0.82 (0.67–0.96)	44 (29–59)*	54 (29–77)†
Gomez-Montes[19]	2014	GA+ *z* score AAo + *z* score isthmus (3VT view) + PV/AV (≤28 wk)	0.85 (0.73–0.98)	40 (26–54)*	64 (39–84)†
Gomez-Montes[19]	2014	TV/MV ratio + MPA/AAo ratio (>28 wk)	0.84 (0.67–1.00)	63 (31–86)*	43 (30–58)†
Gomez-Montes[19]	2014	GA+ *z* score AAo + *z* score AoI (3VT view) + PV/AV (>28 wk)	0.90 (0.83–0.96)	44 (19–73)*	82 (69–90)†

AAo indicates ascending aorta; AD, arterial duct; AoI, aortic isthmus; AUC, area under the curve; AV, aortic valve; CHD, congenital heart defect; CI, confidence interval; d, diameter; DAo, descending aorta; GA, gestational age; IDA, isthmus-ductal angle; IDD, isthmus-ductal diameter; LV, left ventricle; MPA, main pulmonary artery; MV, mitral valve; PV, pulmonary valve; RV, right ventricle; TAoA, transverse aortic arch; TV, tricuspid valve; and 3VT, 3 vessels and trachea.

Familiari, A. et al. Circulation. 2017

Background – Pilot Study

Utility of novel fetal echocardiographic morphometric measures of the aortic arch in the diagnosis of neonatal coarctation of the aorta†

Bhawna Arya*, Aarti Bhat, Margaret Vernon, Jeffrey Conwell and Mark Lewin

Division of Pediatric Cardiology, Seattle Children's Hospital and the University of Washington School of Medicine, Seattle, WA, USA
*Correspondence to: Bhawna Arya. E-mail: bhawna.arya@seattlechildrens.org
†Presented at the American Society of Echocardiography Scientific Sessions, 2014, Portland, Oregon.

- We published novel morphologic measures of the aortic arch to detect coarctation prenatally from 1/2007-1/2014
  - N=60
    - 40 with prenatal suspicion for CoA, 20 confirmed postnatally
    - 20 healthy control fetuses

Seattle Children's HOSPITAL • RESEARCH • FOUNDATION

UW Medicine
UW SCHOOL OF MEDICINE

Arya, B. et al. Prenat Diagn. 2016

Background – Pilot Study

AAo.DAo Angle

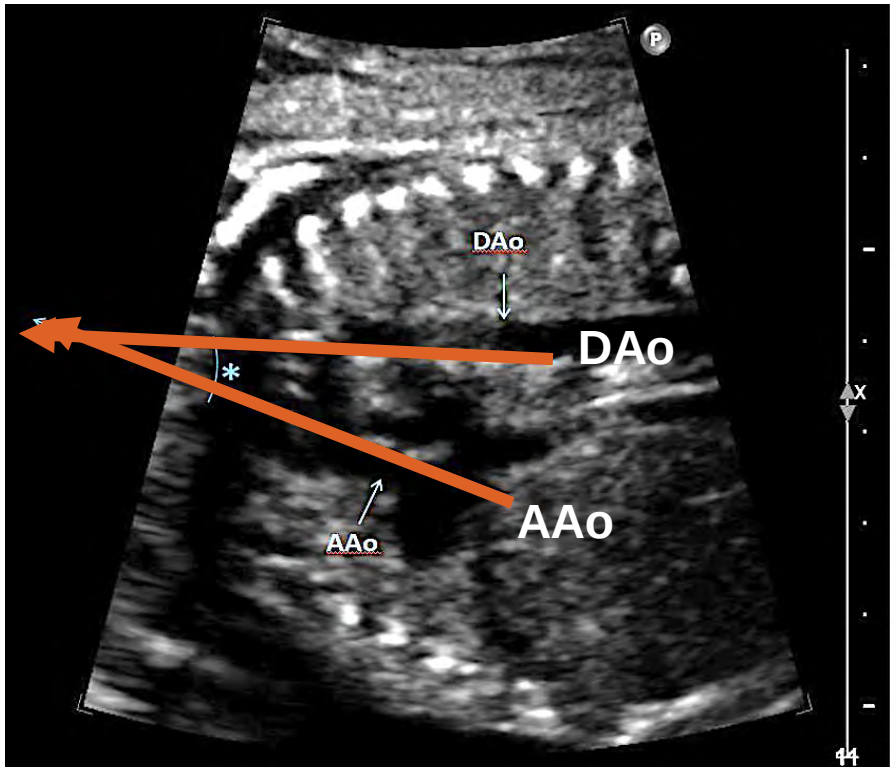


Figure 1A

TAo.DAo Angle

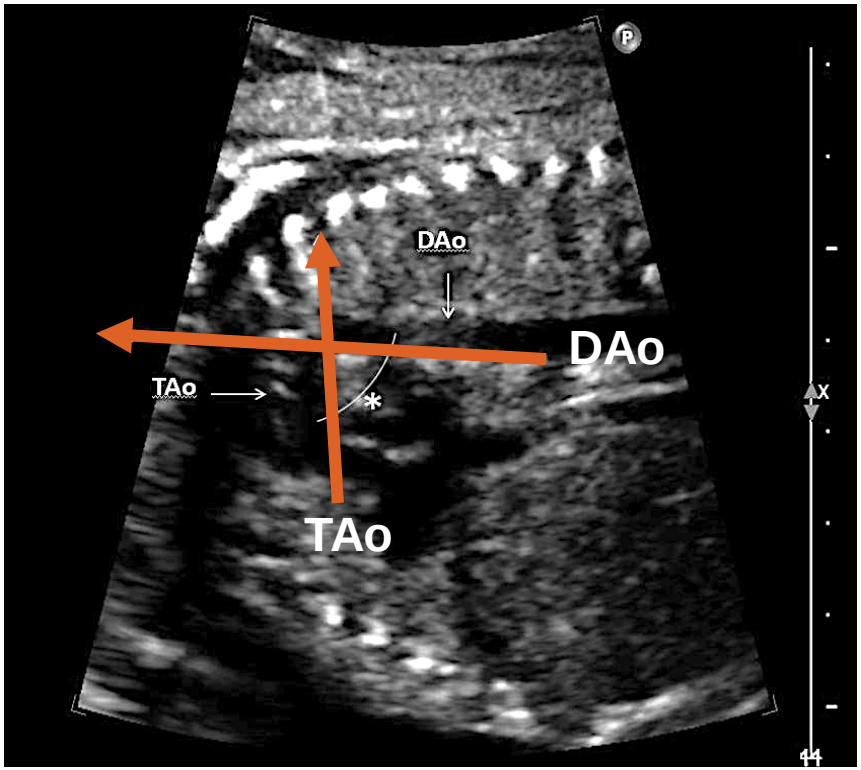


Figure 1B

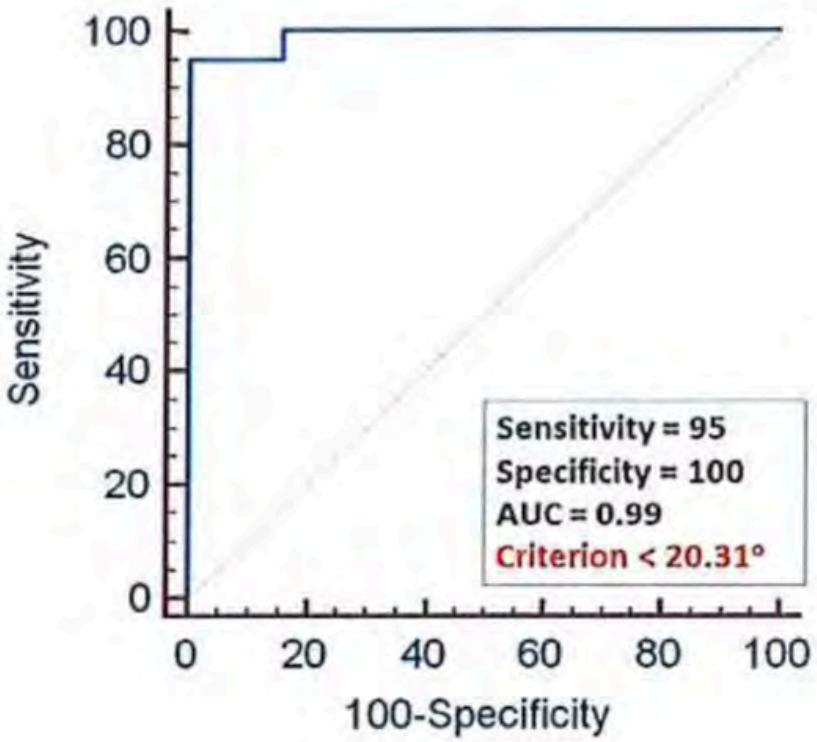
Seattle Children's HOSPITAL • RESEARCH • FOUNDATION

UW Medicine
UW SCHOOL OF MEDICINE

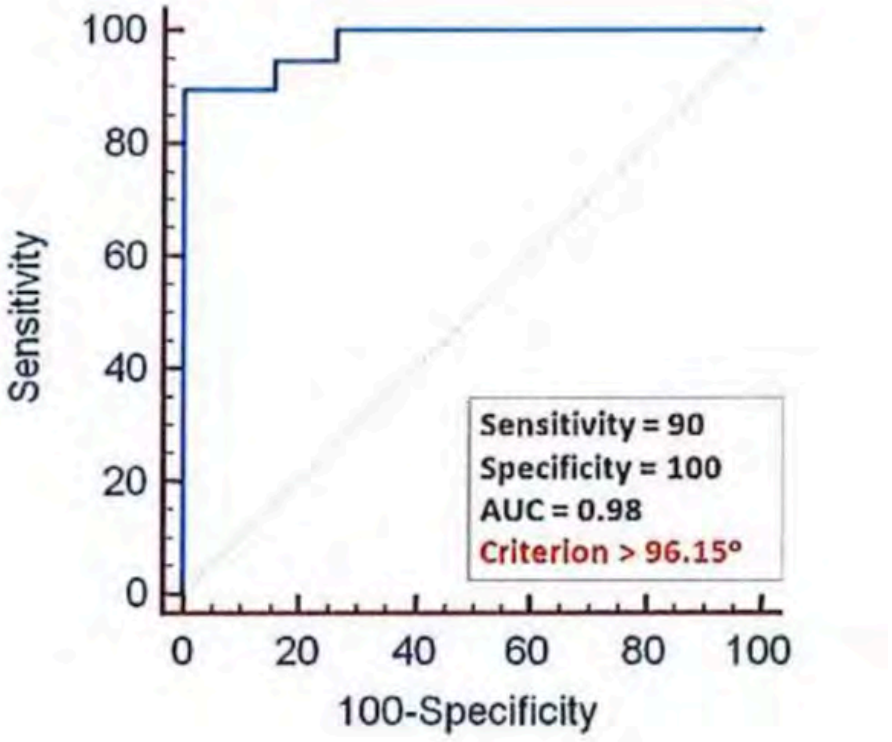
Arya, B. et al. Prenat Diagn. 2016

Results – Pilot Study

AAo.DAo Angle



TAo.DAo Angle



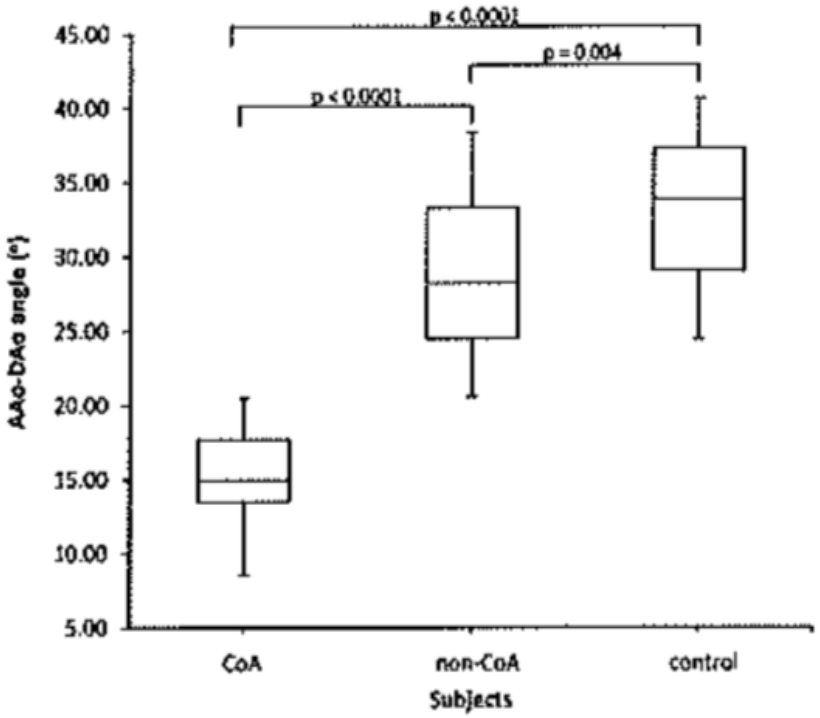
Seattle Children's HOSPITAL • RESEARCH • FOUNDATION

UW Medicine
UW SCHOOL OF MEDICINE

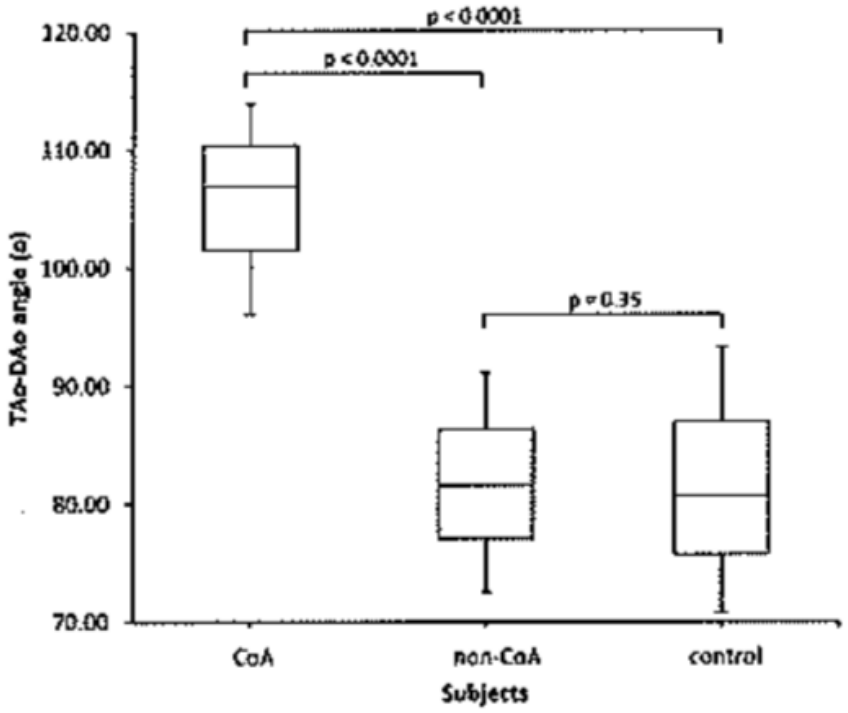
Arya, B. et al. Prenat Diagn. 2016

Results – Pilot Study

AAo.DAo Angle



TAo.DAo Angle



Seattle Children's HOSPITAL • RESEARCH • FOUNDATION

UW Medicine UW SCHOOL OF MEDICINE

Arya, B. et al. Prenat Diagn. 2016

Results – Pilot Study

$$Probability\ of\ cCoA = \left(\frac{1}{1+\exp(-F)}\right)$$

$$F = -17.6 - (0.88\ X\ AAoDAo\ angle) + (0.39\ X\ TAoDAo\ angle)$$

Seattle Children's HOSPITAL • RESEARCH • FOUNDATION

UW Medicine UW SCHOOL OF MEDICINE

Arya, B. et al. Prenat Diagn. 2016

Results – Pilot Study

- Inter-rater variability using interclass coefficients was 0.90 for the TAo.DAo and 0.75 for AAo.DAo
- Angles did not vary through gestation
- A sub group analysis of all fetal echos under 24 weeks showed equivalent predictability

Seattle Children's HOSPITAL • RESEARCH • FOUNDATION

UW Medicine UW SCHOOL OF MEDICINE

Arya, B. et al. Prenat Diagn. 2016

Background – Validation Study

- Given how encouraging our preliminary data was, we pursued a validation study to test this model in a new cohort of patient
- Our new methodology is very different than what has been practiced for decades
- Thus we felt our small pilot study needed to be validated in order to stand up to these more accepted methods

Hypothesis #1

We hypothesize that our two novel measurements will result in more accurate prenatal identification of coarctation of the aorta while decreasing the false-positive rate, compared to standard measurements

Hypothesis #2

We hypothesize that creating a combined multiregression model, utilizing our angle measurements and the standard measures, would provide better predictive power than either method alone

Methods

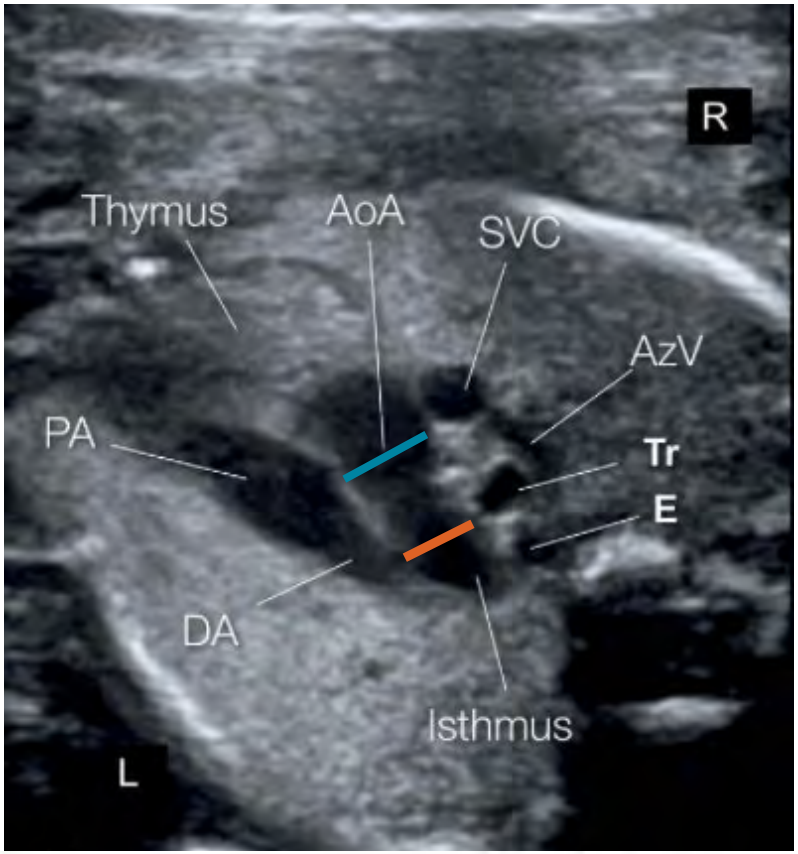
- Retrospective case control study of fetuses with prenatal suspicion for coarctation from 2/2014-9/2018
- Postnatal coarctation was defined as need for prostaglandin at the time of surgery

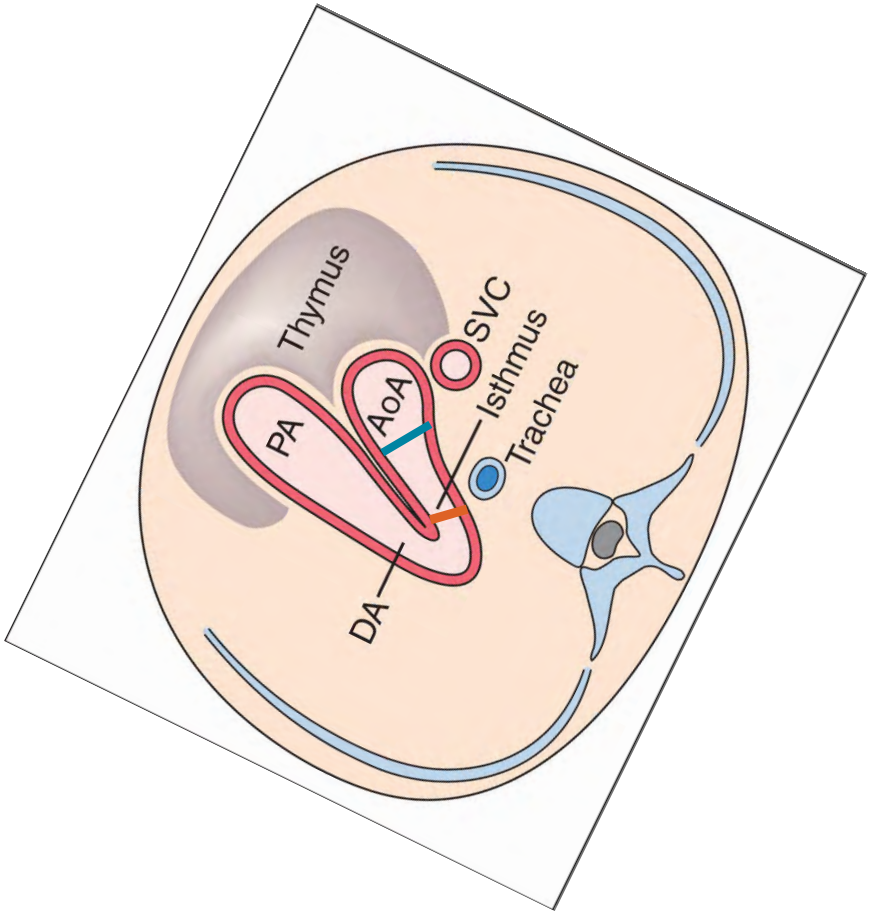
Methods

- Measurements from 1st prenatal echo included:
  - Ascending-descending Ao angle (AAo.DAo)
  - Transverse-descending Ao angle (TAo.DAo)
  - Standard measures:
    - z-scores of aortic isthmus in the sagittal (AoI-sag) aortic isthmus in the three-vessel view (AoI-3VV) and ascending aorta (AAo)

Methods

- Standard Measures: 3VV-isthmus, ascending aorta



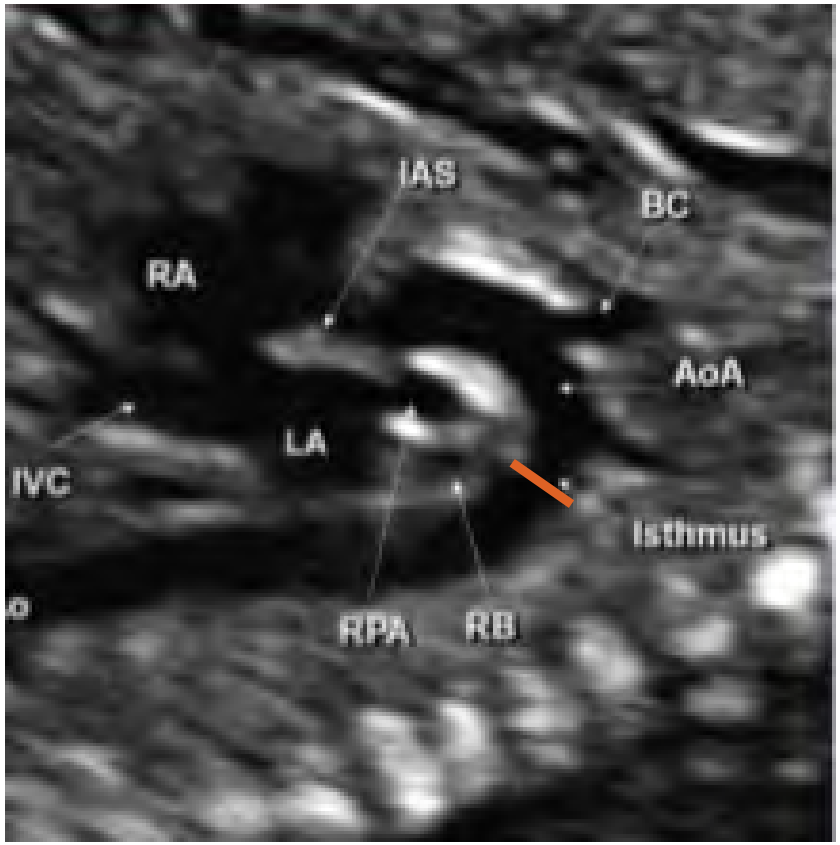


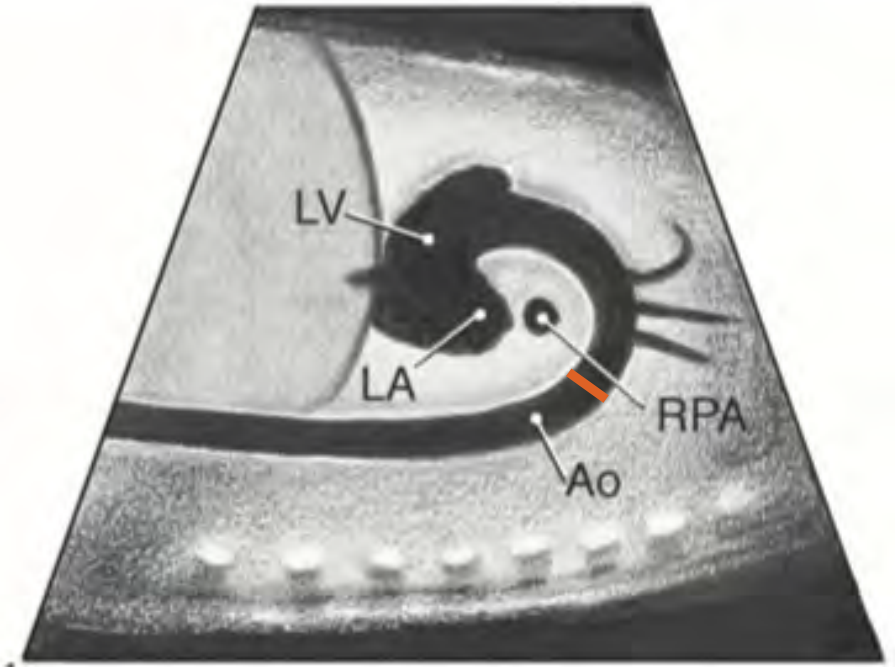
Seattle Children's
HOSPITAL • RESEARCH • FOUNDATION

UW Medicine
UW SCHOOL OF MEDICINE

Methods

- Standard Measures: Sagittal-isthmus





Seattle Children's
HOSPITAL • RESEARCH • FOUNDATION

UW Medicine
UW SCHOOL OF MEDICINE

Methods

- We calculated the probability of coarctation using our previously described multiregression model compared to the standard models described by Gomez-Montes

- Models were compared using ROC curves and PPV and NPV

Results

- Thirty five fetuses met inclusion criteria
  - 10 controls with normal pre- and post-natal echo were included (N=45)
- Coarctation was confirmed in 28/35 neonates
- During the study period, no fetuses with prenatal echocardiograms had a missed diagnosis of CoA

Results

Measurement	PPV	NPV
AAo.DAo+TAo.DAo	79%	83%
AAo+AoI-3VV	86%	60%
AoI-sag+AoI-3VV	78%	85%

Results

AAo-isthmus (3VV) z-scores vs. AAo.DOa + TAo.DAo angles

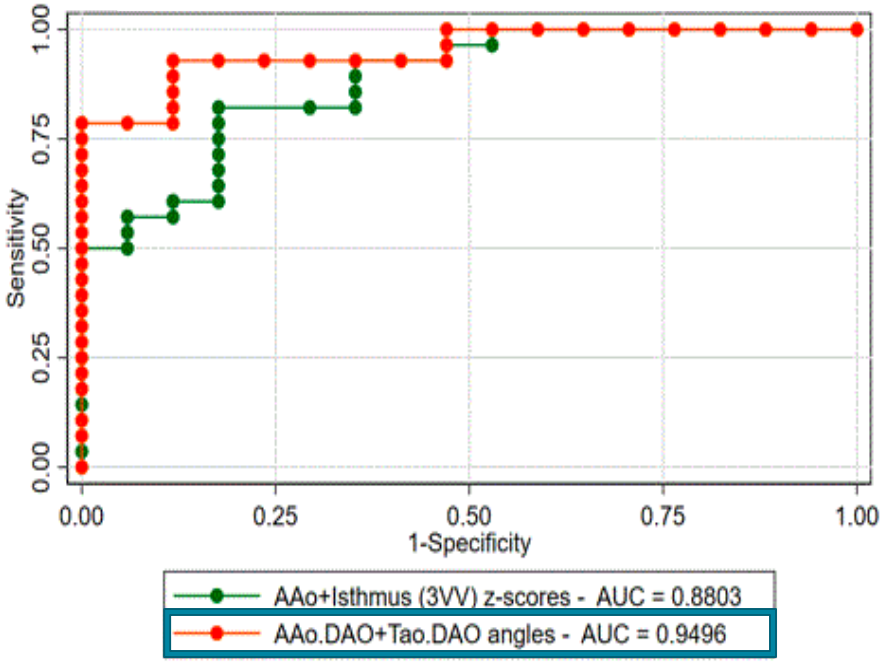


Figure 2a

Isthmus(sag) + Isthmus(3VV) z-scores vs. AAo.DOa+TAo.DAo angles

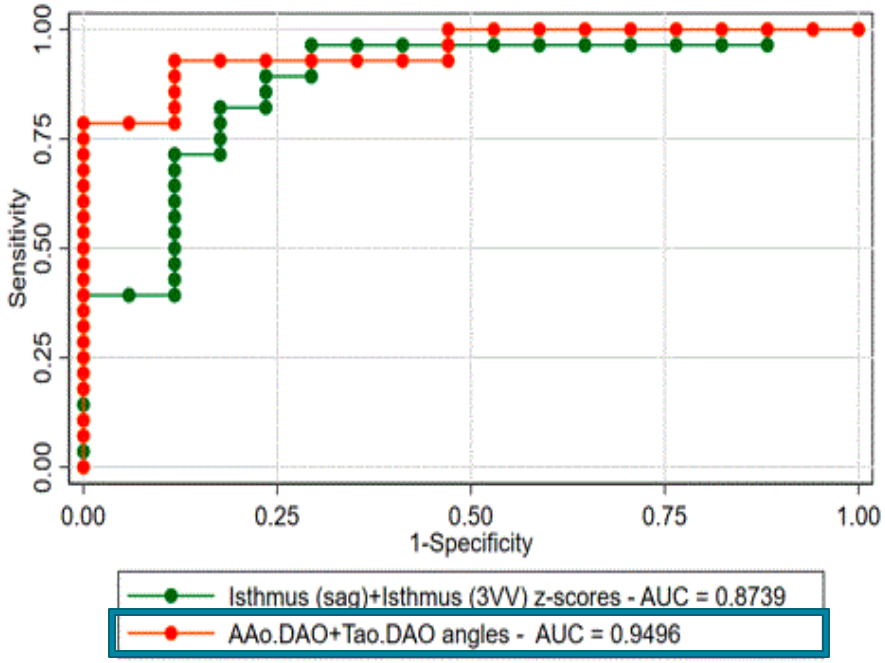


Figure 2b

Seattle Children's HOSPITAL • RESEARCH • FOUNDATION

UW Medicine
UW SCHOOL OF MEDICINE

Results

- Our data suggests that our angle model is equivalent if not slightly improved compared to what is currently accepted

- More importantly, a multiregression model combining all 3 models (consisting of 5 variables) greatly improves the predictive power with a **PPV of 100%** and a **NPV of 85%**

Results

$$Probability\ of\ CoA = \frac{1}{1 + \exp(-F)}$$

$$F = -1.2214 + (AoIsag * 0.0560) + (AoI3VV * -0.0907) + (AAo *$$

Conclusion

- Our study shows that aorta angle measures demonstrate a superior probability model compared to more standard methods of predicting coarctation

- **A combined multiregression model maintains the accuracy of diagnosing coarctation (NPV 85%) while eliminating false positives (PPV 100%)**

Limitations

- Small single center patient population
- Retrospective data – though prenatal measurements still blinded to outcome
- Variation in measurements among different observers – however inter-rater variability was good
- No echo measurement is taken in isolation so this discounts the effect of other variables on interpretation

Future Directions

- Make this model a part of standard practice at Seattle Children's Hospital
- Start obtaining prospective data from these patients to determine the success of this model in real time
- Consider multi-center studies to assess efficacy in a larger population of patients
- Create a scoring system to use these methods in conjunction with other variables

Seattle Children's
HOSPITAL • RESEARCH • FOUNDATION

UW Medicine
UW SCHOOL OF MEDICINE

Acknowledgements

- Thank you to my mentor, Dr. Bhawna Arya and the rest of my co-authors for all of your help throughout this process!

Seattle Children's HOSPITAL • RESEARCH • FOUNDATION

UW Medicine
UW SCHOOL OF MEDICINE

Seattle Children's®
HOSPITAL • RESEARCH • FOUNDATION

Thank You!

Kaitlyn.freeman@seattlechildrens.org

Seattle Children's®

HOSPITAL • RESEARCH • FOUNDATION

Potential Questions from first study

- The fetal echo measurements that demonstrated the most significant differences between CoA and non CoA subjects were measured on the first fetal echo available for each patient and a sub group analysis was performed on fetal echos under 24 weeks which did not show any difference from the final fetal echo.
- There was a 50% false positive rate among this group.
- Mean gestational age at final fetal echo was 32 +/- 4 weeks which did not differ between CoA and non-CoA patients.
- Mild hypoplasia of the mitral and aortic valves (z-score -2 to -4) did not matter.
- Among non-CoA patients and control patients there was a significant difference in the Aao.Dao angle.

References

1. Arya, B. et al. Utility of novel fetal echocardiographic morphometric measures of the aortic arch in the diagnosis of neonatal coarctation of the aorta. Prenat Diagn. 2016 Feb; 36(2): 127–134.
2. Gomez-Montes E. et al. Gestational age-specific scoring systems for prediction of coarctation of the aorta. Prenat Diagn. 2014;34:1198-1206.
3. Familiari, A. et al. Risk Factors for Coarctation of the Aorta on Prenatal Ultrasound. Circulation. 2017 Feb 21;135(8):772-785
4. Liberman, K. et al. Delayed Diagnosis of Critical Congenital Heart Defects: Trends and Associated Factors. Pediatrics. 2014 Aug; 134:2.