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The role of regional prenatal cardiac screening for congenital heart disease: A single center experience

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Abstract

Background: Accurate prenatal diagnosis of congenital heart disease (CHD) allows for appropriate delivery and postnatal management. Geographic constraints limit access to fetal cardiology subspecialists. In our approach, general pediatric cardiologists are first line in regional prenatal cardiac screening. We aim to demonstrate the utility of this approach in diagnosing CHD requiring cardiac interventions within 30 days of life.

Methods: This is a retrospective review of fetal echocardiograms performed at Seattle Children's Hospital regional cardiology sites (SCH-RC) from December 2008 to December 2015. Referrals to Seattle Children's Hospital Prenatal Program (SCH-PNP) were evaluated for referral timing, indication, diagnostic accuracy, and postnatal care. Diagnostic accuracy was determined using the initial postnatal echocardiogram as the gold standard. Major discrepancy was defined as one resulting in change in surgical management.

Results: Of 699 fetuses evaluated at regional sites throughout Washington and Alaska, a small subset (n = 48; 6.9%) required referral to SCH-PNP. Need for relocation was confirmed in 31 subjects, of which 27 required cardiac intervention within 30 days of life. Of those not referred to SCH-PNP (n = 643, 91.9%), none required neonatal cardiac intervention. There were 22 regional diagnostic discrepancies (31% major, 7% minor). Referral to SCH-PNP improved diagnostic accuracy (2% major, 0% minor).

Conclusions: Regional prenatal cardiac screening demonstrated 100% sensitivity and 98.9% specificity for identifying critical CHD. Utilizing regional pediatric cardiologists as first line in prenatal screening in geographically remote regions may improve access to care and outcomes in neonates with critical CHD while improving resource utilization.

KEYWORDS

access to care, fetal echocardiography, prenatal cardiac screening, regional pediatric cardiology

1 | INTRODUCTION

Fetal echocardiography is a valuable tool for identifying critical congenital heart disease (CHD; requiring neonatal intervention within 30 days of age)¹ in utero which in turn allows for preparation of both the expectant family and the medical team who will care for the neonate. Many studies highlight the importance of fetal diagnosis of CHD, but few have demonstrated an improvement in survival.^{2–7} Morris et al. proposed that these studies may not account for infants who died before transfer to a tertiary care center or before surgical intervention. They demonstrated that longer drive time to a cardiac surgical center was associated with higher pretransport and presurgical mortality in hypoplastic left heart syndrome patients compared with those delivering near these centers.⁸ The birth of a neonate with critical CHD may be rare in geographically remote hospitals and prostaglandin E1 may not be available. In a study by Moffett et al. the time to appropriate care for infants with CHD was directly related to morbidity.¹ Geographic constraints limit access to specialized fetal cardiologists for

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many pregnant women.^{9,10} Thus, there is a subset of neonates with undiagnosed critical CHD born in regions that are geographically distant from a tertiary care center, that are at risk for delayed recognition of their disease, inadequate hospital equipment for critical CHD management, and delayed transfer for appropriate medical management.

Seattle Children's Hospital (SCH) is the referral center for a geographically large region, which includes remote areas where access to prenatal care and screening is variable. In an effort to increase the prenatal diagnosis of CHD, the Seattle Children's Heart Center has developed a unique strategy for regional fetal echocardiography outreach to these regions. Screening fetal echocardiograms and consultations are performed by general pediatric cardiologists (with minimal or no formal subspecialty training in fetal cardiac imaging) at Seattle Children's Hospital Regional Cardiology sites (SCH-RC) in Southern and Eastern Washington and Anchorage, Alaska with referral to the Seattle Children's Prenatal Diagnosis and Treatment Program (SCH-PNP) reserved for those in whom a more detailed evaluation is needed or critical CHD is identified. We aim to demonstrate the utility of our regional prenatal cardiac screening strategy for improving identification of critical CHD in remote areas, thereby facilitating transfer of care to a tertiary care center for timely neonatal cardiac intervention.

2 | METHODS

This is a retrospective review of all fetal echocardiograms performed at SCH-RC sites between December 2008 and December 2015. The study was approved by the Seattle Children's Hospital Institutional Review Board. In the majority of cases, obstetricians or maternal fetal medicine providers initiated referrals to our regional pediatric cardiologists for prenatal cardiac screening. Referrals to our tertiary care center, SCH-PNP, were driven by our regional pediatric cardiologists for the majority of cases; a small number of cases were seen at SCH-PNP first and then referred to SCH-RC for future visits. Fetal echocardiograms performed at all sites followed the SCH-PNP fetal echocardiogram protocol, which were based on the2004 American Society of Echocardiogram, and Standards for the Performance of Fetal Echocardiogram.

Maternal records were reviewed to extract clinical data including initial referral indication for prenatal cardiac screening at SCH-RC and fetal cardiac diagnosis. Subjects referred to SCH-PNP were then evaluated for referral indication, fetal cardiac diagnosis at SCH-PNP and delivery plan (including need for transfer of care to SCH-PNP). Neonatal records were evaluated for postnatal diagnosis, type and timing of cardiac intervention, and clinical outcome. A separate evaluation was performed on subjects prenatally and/or postnatally diagnosed with ventricular septal defect (VSD). Although the identification of ventricular septal defects (VSD) is an accepted limitation of fetal echocardiography, we felt it important to account for this group in our population. For fetuses seen at SCH-RC and not referred to SCH-PNP, we attempted to identify prenatally missed CHD by querying the Seattle Children's Hospital (SCH) electronic medical record using the mother's name in the "Patient/Family contact" field. This method would capture any postnatal inpatient or outpatient Cardiology visits at SCH and the SCH-RC clinics. Subjects who required cardiac intervention were divided into neonatal (<30 days of age) and non-neonatal cardiac intervention. Within the neonatal intervention group, we assessed for delays in transfer/intervention as well as overall morbidity and mortality.

Finally, diagnostic accuracy of SCH-RC and SCH-PNP fetal cardiac diagnoses was determined using the findings of the initial postnatal echocardiogram as the gold standard. Major discrepancy was defined as one that resulted in a modification of the postnatal management plan, namely timing of transfer to a tertiary care center or type of cardiac intervention. Minor discrepancy was defined as one that did not result in a change to clinical management.

3 | RESULTS

The SCH-RC clinic locations and cardiologist experience level is described in Figure 1. There were 8 SCH-RC cardiologists over the study period, all of whom had a 3-year pediatric cardiology fellowship. All but one of the SCH-RC cardiologists had completed informal training in fetal cardiology (fetal courses and shadowing experiences), but none had any formal fetal cardiology training. The fetal echocardiograms were primarily performed by pediatric cardiac sonographers with no formal training in fetal echocardiography. They each performed fetal echocardiographers wito had successfully completed the Fetal Examination under Registered Diagnostic Cardiac Sonographers. There were three SCH-RC cardiologists who acquired additional images if needed.

There were 699 fetal subjects seen for prenatal cardiology consultation at one of the SCH-RC sites (mean gestational age at initial consultation 26.5 ± 4.0 weeks); 9% in Alaska (n = 60), 49% in Southerm Washington (n = 342), and 42% in Eastern Washington (n = 297). The prenatal and postnatal course for the population is depicted in Figure 2, the referral indication to SCH-RC for screening echocardiogram in Figure 3, and the referral indication to SCH-PNP in Figure 4.

3.1 Regional cardiology referral patterns

Subject demographics by region are detailed in Table 1. Of the 699 subjects seen at a SCH-RC, only 48 (6.9%) were referred to SCH-PNP for evaluation by a fetal cardiology subspecialist (mean gestational age at initial consultation 30.7 ± 4.3 weeks) for critical CHD requiring relocation for specialized care (n = 31), suspected CHD requiring further diagnostic clarity (n = 11), or difficulty visualizing the fetal heart (n = 6). Critical CHD and need for relocation prior to delivery was confirmed by SCH-PNP evaluation in a total of 31 (4.4%) of the 48 fetuses. Of these 31 subjects, 25 underwent neonatal intervention. The remaining 6 included one subject who remained on prostaglandin E1 and had delayed aortopulmonary shunt placement (day of life 33) due to prematurity, a second with pulmonary atresia, ventricular septal defect, and confluent pulmonary arteries supplied by aortopulmonary collaterals who was discharged with stable circulation, and a third with complex single ventricle anatomy and obstructed total anomalous pulmonary venous return whose care was redirected following delivery. Postnatal



Distance to SCH-PNP (miles)	Years in Practic	
Anchorage, Ala	ska (2 providers)	
2,264	Provider A: 27 Provider B: 16	
Tacoma, Washin	gton (4 providers)	
41	Provider A: 25 Provider B: 20 Provider C: 6 Provider D: 2	
Eastern Washing	gton (2 providers)	
Yakima = 148	Provider A: 41 Provider B: 29	
Tricities = 218		



FIGURE 1 Seattle Children's Hospital Regional Clinic demographics and map

data was not available for the remaining three due to the intrauterine demise of two (both with severe Ebstein's anomaly) and a single pregnancy termination (total anomalous pulmonary venous return).

An additional eight subjects (1.2%) were initially referred to SCH-PNP by the obstetrician either due to family request or concern for significant anomalies. These subjects were then referred by the SCH-PNP regionally for future follow-up. Two subjects had single ventricle physiology and required transfer of care to SCH at 36 weeks' gestation and ultimately underwent neonatal cardiac intervention, but were referred to their local SCH-RC for more convenient interim prenatal follow-up. There were 5 subjects that had CHD requiring prenatal and postnatal cardiology follow-up without neonatal cardiac intervention, and one had a normal evaluation prenatally, but was seen postnatally for family history of left-sided CHD.

Of the 643 cases not referred to SCH-PNP, none required neonatal intervention. Regional prenatal screening demonstrated 100% sensitivity and 98.9% specificity of identifying CHD requiring neonatal cardiac intervention.

3.2 Diagnostic accuracy of regional fetal cardiac screening

We evaluated the 48 subjects referred to SCH-PNP for regional diagnostic accuracy, using the postnatal echocardiogram as the gold

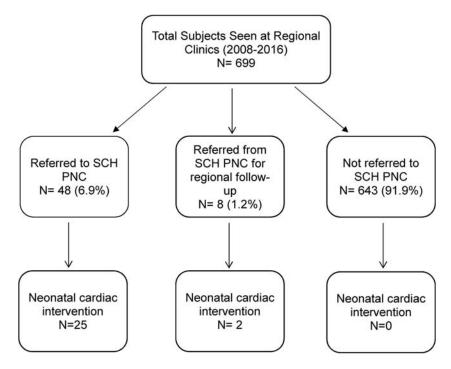


FIGURE 2 Subject prenatal and postnatal clinical course

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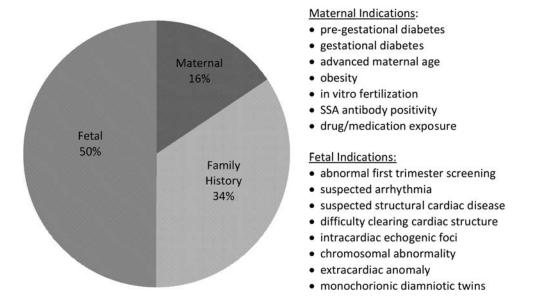


FIGURE 3 Reason for referral to Seattle Children's Hospital Regional Clinics for screening fetal echocardiogram (n = 699)

standard comparison. A total of 26 regional diagnostic discrepancies were identified and 15 (31%) met major discrepancy criteria when comparing the regional prenatal and postnatal diagnosis (Table 2). Referral to SCH-PNP improved diagnostic accuracy with only one major discrepancy (2%), a missed diagnosis of total anomalous pulmonary venous return (TAPVR) in a fetus with known hypoplastic left heart syndrome. There were 10 (7%) minor discrepancies found between regional prenatal diagnoses and postnatal (Table 3). These did not result in a change in surgical planning or counseling. Of those referred to SCH-PNP for diagnosis, there were no minor discrepancies.

There were 17 fetuses with prenatal diagnosis of VSD, 12 of which had postnatal confirmation. There were an additional 11 subjects who

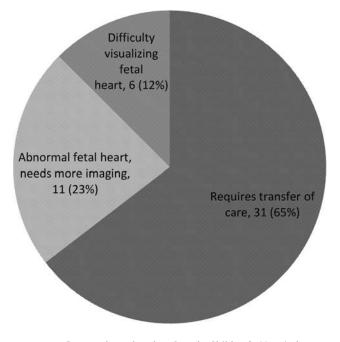


FIGURE 4 Reason for referral to Seattle Children's Hospital Prenatal Program (n = 48)

had a normal fetal echocardiogram in whom a VSD was diagnosed postnatally. None of these subjects required neonatal intervention under 30 days of age and one required surgical VSD closure at 4 months of age and is included in the major discrepancies evaluation.

3.3 Postnatal outcomes and follow-up

Of the 48 patients referred to the SCH-PNP, 29 (60%) were referred postnatally back to their primary regional pediatric cardiologist for further care and two patients required no further follow-up. There were 8 patients that remained in the care of SCH for complex medical care with other comorbidities or for care by our single ventricle clinic or heart failure/transplant team. There were 9 mortalities, 7 were secondary to complications of extracorporeal membrane oxygenation and two were managed with comfort care due to the complexity of their CHD. No deaths were related to delayed or missed diagnosis.

4 | DISCUSSION

Our regional prenatal cardiac screening strategy in geographically remote regions provided care to nearly 700 fetuses over a 7-year period, with 100% sensitivity and 98.9% specificity of identifying critical CHD. All fetuses requiring neonatal cardiac intervention were appropriately referred to the SCH-PNP and delivered near our tertiary care center. There were no delayed diagnoses or unanticipated transfers and ultimately, no mortality associated with our strategy.

This approach increases access to care in geographically distant regions and improves allocation of specialty prenatal cardiology resources to those patients truly requiring it; while saving families from unnecessary travel and associated expenditures. Numerous indications for referral for fetal cardiac evaluation exist though many of these indications are estimated to carry a less than 5%-10% risk of CHD compared to 0.3%-1.2% in the general population.¹¹ Still, the prevalence of CHD in fetuses referred for prenatal cardiology evaluation is high.¹² As

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Location	Mean gestational age (weeks) first visit - regional	Mean gestational age (weeks) first visit - SCHPNP	Total prenatal visits	Mean gestational age at birth (weeks)	Mean age (days) at neonatal surgery	Mean age (days) at non-neonatal surgery
Alaska n=10	26.3 ± 3.3	33.3 ± 5	3.2	38.9± 0.7	5.1 ± 2.93 (n=9)	144 (n=1)
Southern WA n=12	26.8 ± 5	29.2 ± 3.4	2.9	37.7 ±2.9	5.5 ± 3.93 (n=6)	113.6 ± 82.61 (n=5)
Eastern WA n=26	$\textbf{27.3} \pm \textbf{3.9}$	29.7 ± 3.8	1	$\textbf{38.1} \pm \textbf{1.1}$	4.5 ±1.93 (n=8)	93 ± 47.43 (n=4)
SCH-PNP n=8	31.8 ± 1.8	21.6 ± 1.2	2.5	39 ± 0.07	3.5 ± 3.54 (n=2)	129 (n=1)

TABLE 1 Referrals to Seattle Children's Hospital Prenatal Program broken down by regions

the indications for fetal cardiology referral increase, so does the burden on the medical system to provide care to these patients and this strategy becomes even more pertinent to fetal cardiac care. In our experience, only 6.9% of the fetal cardiac screenings resulted in a referral to SCH-PNP and 3.9% required neonatal cardiac intervention. There were 643 pregnant women who received prenatal cardiac evaluation by our general pediatric cardiologists at regional sites, forgoing the time and financial burden of arranging travel to SCH for ultimately low risk fetuses. Fetal echocardiographic diagnoses in the hands of specialized fetal cardiologists practicing at tertiary care centers results in between 8.1% to 10.6% major discrepancies and 18.7% minor discrepancies when compared to the postnatal diagnosis.^{13–17} The SCH-RC demonstrated a higher rate of major discrepancies and similar minor discrepancies compared with the published data, 31% and 7%, respectively. Our regional pediatric cardiologists have significant time constraints for prenatal cardiology visits and both the physicians and cardiac sonographers have limited or no formal training in fetal cardiology. The

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Regional diagnosis (discrepancy in bold)	Postnatal diagnosis (discrepancy in bold)	SCH-PNP discrepancy
Truncus arteriosus or TOF/pulmonary atresia	TOF, severe PS, MAPCAs	No
Large VSD	IAA, large VSD	No
Single ventricle with aortic valve atresia	Heterotaxy, single ventricle, pulmonary atresia, MAPCAs, supracardiac TAPVR	No
Single ventricle, DORV, d-TGA physiology	Tricuspid atresia, d-TGA, VSD	No
Hypoplastic left heart syndrome	Hypoplastic left heart syndrome and TAPVR	No
Suspected normal, could not clear aortic arch	Truncus arteriosus	No
Mildly hypoplastic left heart, possible coarctation	Normal	No
RV dominant CAVSD , aortic atresia , aortic arch hypoplasia	Heterotaxy, RV dominant CAVSD, DORV, d-TGA physiology, pulmonary atresia, mixed TAPVR	No
Truncus arteriosus	TOF, severe PS, confluent PAs, MAPCAs	No
DORV, d-TGA physiology, mild PS	Heterotaxy, dextrocardia, cor triatriatum, CAVSD, DORV, L-TGA physiology, PS	No
DORV versus TOF	Large anterior malalignment VSD	No
Heterotaxy, dextrocardia, LV dominant CAVSD, d-TGA, mild PS	Heterotaxy, dextrocardia, RV dominant CAVSD, TAPVR	Yes
Right and left ventricular size discrepancy, poorly visualized aortic arch and pulmonary veins	Bicuspid aortic valve, mild mitral valve and aortic arch hypoplasia	No
Tricuspid atresia, d-TGA and possible aortic arch hypoplasia	Tricuspid atresia, d-TGA, type A IAA	No
Normal	Moderate sized posterior malalignment VSD	No SCH visit

Abbreviations: TOF, tetralogy of Fallot; PV, pulmonary valve; PS, pulmonary valve stenosis; PAs, pulmonary arteries; MAPCAs, major aortopulmonary collateral arteries; VSD, ventricular septal defect; IAA, interrupted aortic arch; TAPVR, total anomalous pulmonary venous return; DORV, double outlet right ventricle; d-TGA, dextro-transposition of the great arteries; CAVSD, complete atrioventricular septal defect.

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Regional diagnosis (discrepancy in bold)	Postnatal diagnosis (discrepancy in bold)	SCH-PNP discrepancy
D-TGA	D-TGA, vascular ring	No
Hypoplastic left heart syndrome with VSD	Double outlet right ventricle, mitral atresia, hypoplastic arch	No
Hypoplastic ascending aorta	Normal	No
Normal	Left superior vena cava to coronary sinus	No
Tricuspid atresia, VSD, PS , confluent PAs, tumor in RV	Tricuspid atresia, no VSD , hypertrophied RV, absent pulmonary valve , confluent PAs	No
RV dominant CAVSD, single ventricle with aortic arch hypoplasia, left superior vena cava	RV dominant CAVSD, aortic arch hypoplasia, no left superior vena cava	No
TOF, PS, confluent PAs	TOF, discontinuous left PA	No
TOF/pulmonary atresia with confluent PAs	TOF, PS	No
Heterotaxy, DILV, L-TGA, pulmonary atresia, confluent PAs .	Heterotaxy, DILV, D-TGA, pulmonary atresia, discontinuous PAs	No
CAVSD	CAVSD with left superior vena cava to coronary sinus	No

Abbreviations: d-TGA, dextro-transposition of the great arteries; I-TGA, levo-transposition of the great arteries; VSD, ventricular septal defect; PS, pulmonary valve stenosis; PAs, pulmonary arteries; RV, right ventricle; CAVSD, complete atrioventricular septal defect; TOF, tetralogy of Fallot; DILV, double inlet left ventricle.

echocardiography machines utilized are predominantly utilized for imaging pediatric patients. Although there are specific settings for fetal imaging with appropriate probes, the optimal technology for challenging fetal imaging is not available. These factors likely impact the diagnostic accuracy. Future studies should focus on determining acceptable diagnostic discrepancies for regional pediatric cardiologists performing screening prenatal cardiac evaluation.

Because the institution's digital echocardiogram storage system is shared among the various SCH sites locally and regionally, it is common for our regional cardiologists to review complex CHD diagnoses and technically challenging studies with the SCH-PNP cardiologists. This facilitates referral and management planning. Thus, despite the increased discrepancy rate, in all cases of critical CHD, the regional diagnoses led to appropriate referral and transfer of care to SCH-PNP and there were no mortalities due to delayed diagnosis or transfer. Furthermore, the SCH-PNP diagnostic discrepancies are similar, if not slightly improved compared with the current literature, (2% major and 0% minor discrepancies), thereby improving the accuracy of the prenatal diagnoses.

The majority of subjects referred from SCH-RC to SCH-PNP were postnatally referred back to their primary regional pediatric cardiologists for outpatient follow-up. Regional prenatal cardiac screening established continuity of care between the prenatal and postnatal periods despite the need for tertiary neonatal care. Most patients who remained in the care of the SCH outpatient clinic were instructed to remain locally after hospital discharge due to medical complexity and high mortality risk related to living in distant/remote regions. Patients with single ventricle physiology alternated visits at the SCH single ventricle and regional cardiology clinic. Once they returned home and required less frequent follow-up or interventions, families chose to be seen by the regional cardiologists.

4.1 | Study limitations

The study was limited by the inherent nature of single-center retrospective studies. Evaluation of postnatal outcomes for fetuses not evaluated by the SCH-PNP was extensive within the SCH medical records, however, did not account for patients not seen within the SCH and SCH-RC system. Subjects who died at unaffiliated regional hospitals or birthing centers would not be captured by this analysis, nor would patients evaluated and treated at other pediatric cardiology practices or hospitals. We expect that the number of subjects lost in this analysis, though important, is quite low as SCH is the primary referral site for the regions described.

5 | CONCLUSION

Prenatal cardiac screening performed by regional pediatric cardiologists is effective for diagnosing critical CHD in geographically remote regions, with 100% sensitivity and 98.9% specificity of identifying CHD requiring neonatal cardiac intervention. Furthermore, regional screening reserves specialized prenatal care for the small subset of patients who require more detailed cardiac evaluation. Utilizing general pediatric cardiologists as a first line in prenatal cardiac screening in geographically remote regions may improve access to care, rate of diagnosis, and outcomes in neonates with critical CHD while improving resource utilization.

ETHICAL APPROVAL

This article does not contain any studies with human participants or animals performed by any of the authors.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest with the contents of this article.

AUTHOR CONTRIBUTIONS

Data analysis/interpretation: Pasierb, Peñalver, Vernon, Arya

Drafting article: Pasierb, Arya

Critical Revision and approval of the article: Peñalver, Vernon, Arya Concept/Design: Vernon, Arya

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