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Accuracy of fetal echocardiography: a cardiac segment-specific analysis

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KEYWORDS: accuracy; congenital heart disease; fetal echocardiography; quality assurance

ABSTRACT

Objective *In patients with congenital heart disease, comprehensive, segment-specific analysis of cardiac anatomy has become 'the standard of care', largely as a result of improvements in cardiac imaging technology. Our aim was to apply segment-specific standards to assess the accuracy of fetal echocardiography.*

Methods *This was a retrospective review of all fetal echocardiograms (*n *= 915) performed at our center between August 1998 and June 2003. Of these, 100 studies had congenital heart disease findings and corresponding postnatal studies on the same patients for comparison. An expert independent pediatric echocardiologist, using the standards of accuracy expected of postnatal echocardiography, assessed the studies for the following cardiac segments: abdominal situs, systemic venous return (VR), pulmonary VR, atria, atrioventricular valves, ventricular septum, ventricular hypoplasia, ventricular morphology, semilunar valves, great arterial relation and aortic arch. Sensitivity, specificity, and positive and negative predictive values were calculated for each segment.*

Results *Specificity and negative predictive value were high for all cardiac segments (range, 82–100%). Sensitivity and positive predictive value were similarly high (range, 83–100%) for most cardiac segments, but were only 50–88% for systemic VR, pulmonary VR and aortic arch segments.*

Conclusions *Fetal echocardiography has excellent diagnostic accuracy in describing intracardiac anatomy. However, despite both technological advances and improved physician awareness, assessment of systemic VR, pulmonary VR, and aortic arch anatomy remain challenging.* *Copyright © 2006 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

The general diagnostic accuracy of fetal echocardiography (fetal echo) in detecting or excluding significant fetal heart anomalies has been reported to exceed 80%[1–4], particularly in the hands of experienced perinatal cardiologists[2,5]. Fetal echo has been shown to be particularly accurate in the detection of complex congenital cardiac lesions, such as single ventricular anatomy[6], conotruncal defects[7] and the heterotaxy complexes[8]. With improvements in fetal echo equipment and evolution of fetal cardiology into an interventional discipline, it has become essential to determine the segment-specific diagnostic accuracy of fetal echo.

The Cincinnati Children's Hospital echocardiography laboratory employs a formal quality assurance system for all transthoracic (TTE) and transesophageal (TEE) echocardiographic studies to identify false-positive and false-negative segmental diagnoses. By applying the same critical segment-specific standards used in evaluation of these studies at our center, we aimed to assess the accuracy of fetal echo in fetuses with a wide range of structural cardiac abnormalities and to evaluate whether our accuracy had improved with improvements in technology and increased experience.

METHODS

We reviewed retrospectively all fetal echo studies (n = 915) performed at our center between August 1998 and June 2003. Of these, 100 studies had findings of congenital heart disease and available complete fetal and postnatal TTEs for comparison. Studies were not excluded systematically for any reason. All studies were performed under the supervision of an expert fetal echocardiographer (E.C.M. or R.A.M.) with a minimum of 5 years' experience in performing and interpreting fetal echos.

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Studies were performed using available two-dimensional (2D) and pulsed wave, color flow and power Doppler modalities, with Sonos 5500 and HDI 5000 (Phillips Medical Systems, Andover, MA, USA) and Vivid 5 and 7 (General Electric Corporation, Milwaukee, WI, USA) ultrasound machines. Cardiac imaging views and sweeps were obtained and recorded in accordance with the subsequently published American Society of Echocardiography's 'Guidelines and standards for performance of the fetal echocardiogram'[9].

Using as reference standards the same critical segment-specific standards that are applied to TTE and TEE studies for our center's non-invasive imaging quality assurance system, postnatal TTEs were assessed by an independent expert observer (W.M.G.). The 12 cardiac segments along with the specific criteria assessed within them are listed in Table 1. For each segment, a clinical judgment was made as to whether each diagnosis made on the prenatal study represented a true-positive, true-negative, false-positive or false-negative finding; it was also noted when a segment could not be evaluated due to limited imaging (coded as 'not available'). An example of the level of adherence to the strict standards used for our center's postnatal TTE studies is shown in Table 2. Sensitivity, specificity and positive and negative predictive values were calculated for each segment. The percentage of time a segment could not be evaluated due to technical reasons was also calculated.

To test our suspicions that increases in experience and caseload volume have improved our accuracy during the 5-year time frame, the tabulated results were further subdivided into 'old' (1998–2000, $n = 42$) and 'new' (2001–2003, $n = 58$) cohorts, and these results compared with one another.

Overall results are presented as descriptive data. The frequency with which useful segmental data acquisition was achieved in each cohort (old vs. new) was assessed via chi-square analysis of proportions.

RESULTS

The segments most often evaluated inadequately in the old cohort of prenatal studies were: abdominal situs (24%), systemic venous return (VR; 60%), pulmonary VR (67%), aortic arch (21%) and ductal arch (14%). These percentages fell to 0%, 7%, 9%, 5% and 5%, respectively, in the new cohort (Table 3 and Figure 1). With the exception of the ductal arch, these changes in percentage were statistically significant. The remaining segments were evaluated adequately with $\geq 97\%$ frequency. Overall sensitivity, specificity and predictive values are given in Table 4.

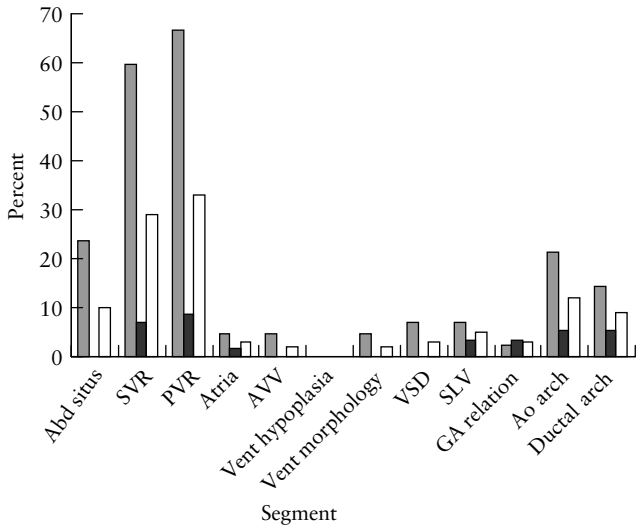

Figure 1 Percentage of patients with segments evaluated inadequately overall (□), and separated into 'old' (1998–2000; ▩) and 'new' (2001–2003; ■) cohorts. Abd, abdominal; Ao, aortic; AVV, atrioventricular valves; GA, great arterial; PVR, pulmonary venous return; SLV, semilunar valves; SVR, systemic venous return; Vent, ventricular; VSD, ventricular septal defect.

Table 1 Specific criteria assessed per cardiac segment

Segment	*Criteria assessed*
1) Abdominal situs	Correct definition
2) Systemic venous return (VR)	Correct identification of systemic VR drainage pattern; correct identification of systemic venous flow aberrancies
3) Pulmonary VR	Correct definition of pulmonary VR; correct identification of pulmonary venous flow abnormalities (e.g. stenoses)
4) Atrial anatomy	Correct definition of atrial situs; correct identification of cor triatriatum membrane or other structural abnormalities of the atrium; correct identification of atrial appendage juxtaposition, if present
5) Atrioventricular valves (AVV)	Correct description of morphology and function of AVV leaflets and associated apparatus
6) Ventricles: interventricular septum	Correct determination of septal integrity or description of size and location of ventricular septal defect(s), if present
7) Ventricles: ventricular hypoplasia	Correct determination of the presence and degree of ventricular hypoplasia
8) Ventricles: ventricular morphology	Correct identification of each ventricle and ventricular looping pattern (-D or -L)
9) Semilunar valves and outflow tracts	Correct identification of presence of subvalvar, valvar or supravalvar stenosis; presence of aortic or pulmonary valve insufficiency
10) Great arterial relations	Correct definition
11) Aortic arch	Correct determination of patency or degree of hypoplasia/obstruction/interruption
12) Ductal arch	Correct determination of ductal patency or degree of obstruction

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Table 2 Example of a coding algorithm used by our center to assess accuracy of postnatal transthoracic echocardiography (TTE) studies

Fetal echo: performed at 28 + 3 weeks' gestation
1) {S,L,L}-transposition of the great arteries with double inlet left ventricle
   a) moderate hypoplasia of right-sided AV valve (6 mm)
   b) small BVF and anterior outlet chamber
   c) normal-sized (9 mm) left AV valve
   d) no significant AV valve insufficiency
2) Small aortic valve
3) Hypoplastic ascending aorta, with antegrade flow
4) Hypoplastic transverse aortic arch
5) Good-sized pulmonary artery and ductus arteriosus

Postnatal TTE: performed on DOL #1
1) {S,L,L}-transposition of the great arteries with double inlet left ventricle
   a) small bulboventricular foramen; BVF area index = 1.4 cm/m^2
   b) aortic annulus (6.5 mm)
      i) no stenosis or insufficiency
   c) pulmonary annulus 7.6 mm
      i) no stenosis or insufficiency
2) Moderate transverse arch (3 mm) and severe (1.7 mm) isthmus narrowing. No gradient on PGE1
3) Normal-sized bilateral AV valves:
   a) right-sided AV valve annulus = 10 mm
      i) redundancy of the right AV valve apparatus, with prolapse of the valve into the subpulmonary area but no current obstruction to flow
   b) left-sided AV valve annulus = 8.5 mm
   c) Trace right atrioventricular valve insufficiency
4) Large patent ductus arteriosus; bidirectional shunt
5) Patent foramen ovale, small–moderate, left to right shunt
6) Confluent branch pulmonary arteries, dimensions (RPA = 5.2 mm; LPA = 6.1 mm).

Analysis/coding:
(1) A false positive (fp) was coded for the atrioventricular valves: the fetal study suggested right atrioventricular valve hypoplasia, which was not present on the postnatal TTE.
(2) A false negative (fn) was coded for the semilunar valves: the fetal study described the aortic annulus as 'small', though it was found to be normal on postnatal TTE. The other segments were coded as either true positive (ventricular hypoplasia, ventricular morphology, ventricular septal defect, great artery relation and aortic arch) or true negative (the remainder).

AV, atrioventricular; BVF, bulboventricular foramen; DOL, day of postnatal life; PGE1, prostaglandin E1; R/LPA, right/left pulmonary artery.

Table 3 Numbers of patients with segments evaluated inadequately

	Number evaluated inadequately			
Segment	*Old (1998–2000)* (n = *42*)	*New (2001–2003)* (n = *58*)	*Overall* (n = *100*)	P *old vs. new*
Abdominal situs	10	0	10	0.0001
Systemic venous return	25	4	29	0.0001
Pulmonary venous return	28	5	33	0.0001
Atria	2	1	3	NS
Atrioventricular valves	2	0	2	NS
Ventricular hypoplasia	0	0	0	NS
Ventricular morphology	2	0	2	NS
Ventricular septal defect	3	0	3	NS
Semilunar valves	3	2	5	NS
Great arterial relation	1	2	3	NS
Aortic arch	9	3	12	0.014
Ductal arch	6	3	9	NS

NS, not significant.

The ability to demonstrate successfully anatomy and specific diagnostic errors for each anatomic segment were as follows. Abdominal situs was described correctly in 90/100 (90%) cases. In nine cases, all from the old cohort, the stomach bubble was not identified and/or recognized on 2D imaging, though it was present on postnatal TTE imaging; in the one remaining case, there was an additional diagnosis of severe tracheoesophageal fistula.

Systemic VR had an overall 13% incidence of false-negative diagnoses. The most commonly missed diagnosis was a left superior vena cava (SVC) draining to either the coronary sinus or the left atrium. Interrupted inferior vena

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Table 4 Sensitivity, specificity and positive (PPV) and negative (NPV) predictive values of fetal echocardiography and prevalence of abnormalities, according to anatomical segment: all data ($n = 100$)

Segment	*Sensitivity (%)*	*Specificity (%)*	*PPV (%)*	*NPV (%)*	*Prevalence (%)*
Abdominal situs	100	99	88	100	8
Systemic venous return	50	97	88	82	30
Pulmonary venous return	75	97	60	98	6
Atria	92	100	100	95	37
Atrioventricular valves	97	89	94	94	61
Ventricular septum	83	87	91	77	60
Ventricular hypoplasia	98	100	100	98	52
Ventricular morphology	95	97	90	99	19
Semilunar valves	89	90	92	86	56
Great arterial relation	92	96	89	97	27
Aortic arch	74	91	82	87	35
Ductal arch	95	96	95	96	48

cava (IVC) and absent right SVC were each missed once. False-positive diagnoses occurred with a 3% frequency, consisting of one false-positive occurrence each of an interrupted IVC and a left SVC.

With respect to the pulmonary veins, there was one (1%) false-negative diagnosis in a case of missed partial anomalous pulmonary venous connection. In two cases (2%) a false-positive diagnosis of anomalous VR to the coronary sinus was made.

There were no false-positive diagnoses for the atria, but two false-negative diagnoses (2%): a common atrium was missed in one instance, and a levoatrial cardinal vein decompressing the left atrium was not diagnosed in a newborn with mitral stenosis.

There were six false-negative atrioventricular (AV) valve diagnoses: mitral valve dysplasia was not recognized in two cases and double inlet AV connection, Ebstein's anomaly of the tricuspid valve, mitral stenosis and cleft mitral valve were each missed on one occasion. There were three false-positive diagnoses: tricuspid atresia (vs. hypoplasia/stenosis), complete (vs. partial) AV septal defect, and a small right AV valve in double-inlet AV connection.

Ventricular morphology was not assigned in 2/100 cases, in both cases in fetuses with single ventricular anatomy and technically poor acoustic windows. The presence of ventricular hypoplasia was correctly identified or excluded in all cases. Ventricular morphology was identified incorrectly in two cases of single ventricular anatomy, the morphology being misassigned as right ventricular and left ventricular in one instance each.

There were false negative ventricular septal diagnoses in 10% of cases; the most frequently missed diagnosis was muscular ventricular septal defect (VSD) ($n = 4$), followed by perimembranous VSD ($n = 3$) and a single case of an unrecognized bulboventricular foramen in the setting of double-inlet LV (DILV). The additional two false-negative cases for the VSD segment were cases in which only one VSD was mentioned in the fetal study, but the postnatal study revealed multiple VSDs. Five false-positive diagnoses included perimembranous VSD ($n = 3$), muscular VSD ($n = 1$) and inlet VSD in the setting of complete AV canal defect (vs. partial AV canal defect with intact ventricular septum, $n = 1$).

For the outflow tracts and semilunar valve anatomy, there were two false-negative diagnoses: in one case the pulmonary valve was described as small at 26 weeks' gestation but was found to be atretic on postnatal echocardiography, and in the other a false-negative diagnosis of a normal pulmonary valve was found to have a mildly hypoplastic annulus. False positives were more common (5% incidence). A small semilunar valve was found to be normal on postnatal echocardiography in three cases, a thickened pulmonary valve was found to be normal in one and pulmonary valve atresia was misdiagnosed as aortic atresia in a patient with double-outlet right ventricle (DORV).

With respect to great arterial relation, there were four false-negative diagnoses: in two cases of hypoplastic left heart syndrome a normal great arterial relation was found to be DORV ($n = 2$), one case of DORV was found to have malposition of the great arteries and in one case of DILV there was transposition. False-positive diagnoses, when the great arterial relation was found to be normal, included transposition of the great arteries in one case of DORV, and in one case of DILV a diagnosis of transposition of the great arteries was found to be a double-outlet single ventricle.

The aortic arch had seven false-negative diagnoses. The most frequently missed diagnosis was a juxtaductal coarctation ($n = 6$), although in four of these the fetal echo false-negative diagnosis was assigned when the fetal study described distal arch hypoplasia, but did not specifically describe coarctation, as is necessary in postnatal TTE (the standard to which we adhered in this analysis). False-positive diagnoses consisted of predominantly coarctation ($n = 4$), with one case in which the diagnosis of small transverse arch with retrograde filling was found to be a patent ductus arteriosus in a patient with DORV and severe pulmonary stenosis.

There were two false-negative diagnoses involving the ductal arches: in one case a left-sided ductus arteriosus was missed in the setting of right aortic arch, and in one case (as described in the preceding aortic arch paragraph),

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Table 5 Sensitivity, specificity and positive (PPV) and negative (NPV) predictive values of fetal echocardiography and prevalence of abnormalities, according to anatomical segment: old cohort (1998–2000; $n = 48$)

Segment	*Sensitivity (%)*	*Specificity (%)*	*PPV (%)*	*NPV (%)*	*Prevalence (%)*
Abdominal situs	100	100	100	100	12.5
Systemic venous return	56	88	83	64	53
Pulmonary venous return	67	100	100	92	21
Atria	90	100	100	97	25
Atrioventricular valves	97	91	97	91	73
Ventricular septum	81	94	94	81	54
Ventricular hypoplasia	96	100	100	94	62
Ventricular morphology	91	97	91	97	28
Semilunar valves	96	83	93	91	69
Great arterial relation	86	96	92	93	34
Aortic arch	71	94	92	75	52
Ductal arch	95	93	95	93	61

Table 6 Sensitivity, specificity and positive (PPV) and negative (NPV) predictive values of fetal echocardiography and prevalence of abnormalities, according to anatomical segment: new cohort (2001–2003; $n = 52$)

Segment	*Sensitivity (%)*	*Specificity (%)*	*PPV (%)*	*NPV (%)*	*Prevalence (%)*
Abdominal situs	100	98	75	100	5
Systemic venous return	50	98	80	92	15
Pulmonary venous return	100	96	33	100	2
Atria	92	100	100	94	46
Atrioventricular valves	97	89	91	96	53
Ventricular septum	84	81	89	74	64
Ventricular hypoplasia	100	100	100	100	45
Ventricular morphology	100	98	89	100	14
Semilunar valves	81	93	91	85	46
Great arterial relation	100	95	86	100	21
Aortic arch	79	90	73	93	26
Ductal arch	95	97	95	97	40

the transverse arch was mistaken for a patent ductal arch in a patient with DORV. The one false-positive diagnosis from this segment was that of mild ductal restriction in a fetus with hypoplastic left heart syndrome, which had a large, patent ductus arteriosus on postnatal echo.

As detailed in Tables 5 and 6 and Figure 2, there were changes in overall segment-specific accuracy in the two time periods studied. For the 'difficult' segments (systemic VR, pulmonary VR and aortic arch), sensitivity increased by an average of 12%, while the negative predictive value increased by an average of 18% with time. There was essentially no change in average specificity for these three segments. There was a noticeable decrease in average positive predictive value (30%) and prevalence (28%) of lesions in these segments.

DISCUSSION

Prior reports have established the ability of fetal 2D and Doppler echo to distinguish normal from abnormal fetal hearts[4,10,11]. There is further evidence establishing the accuracy of fetal echo for identifying specific congenital heart malformations[1–3], such as functional single ventricle[6] and conotruncal anomalies[7], particularly when there is an experienced pediatric cardiologist[5] involved in the study. However, we are unaware of any prior data analysis of the segment-specific accuracy of fetal echo, particularly when held to the higher standards usually reserved for TTE.

This one-center experience demonstrates that fetal echo can describe reliably comprehensive segmental cardiac anatomy, and is highly accurate in doing so when held to the rigorous standards used in the assessment of TTE studies. Detailed analysis showed that, as expected, with increased operator experience, all segments can be evaluated with an acceptable frequency (> 90%).

This frequency even applied to the more difficult segments (systemic and pulmonary VR and aortic arch morphology) and their associated diagnoses. For example, although the elusiveness of fetal coarctation of the aorta has been well recognized[12,13] (particularly when secondary findings such as ventricular size asymmetry are the major study findings), we found, using the rigorous postnatal TTE standard of coarctation diagnosis, that the sensitivity and negative predictive value for this diagnosis improved with increased operator experience over time (with visualization of the aortic isthmus and a coarctation shelf, if present). Nomiyama *et al.*[13] showed that even in late gestation the fetal aortic isthmus could be visualized > 85% of the time, in

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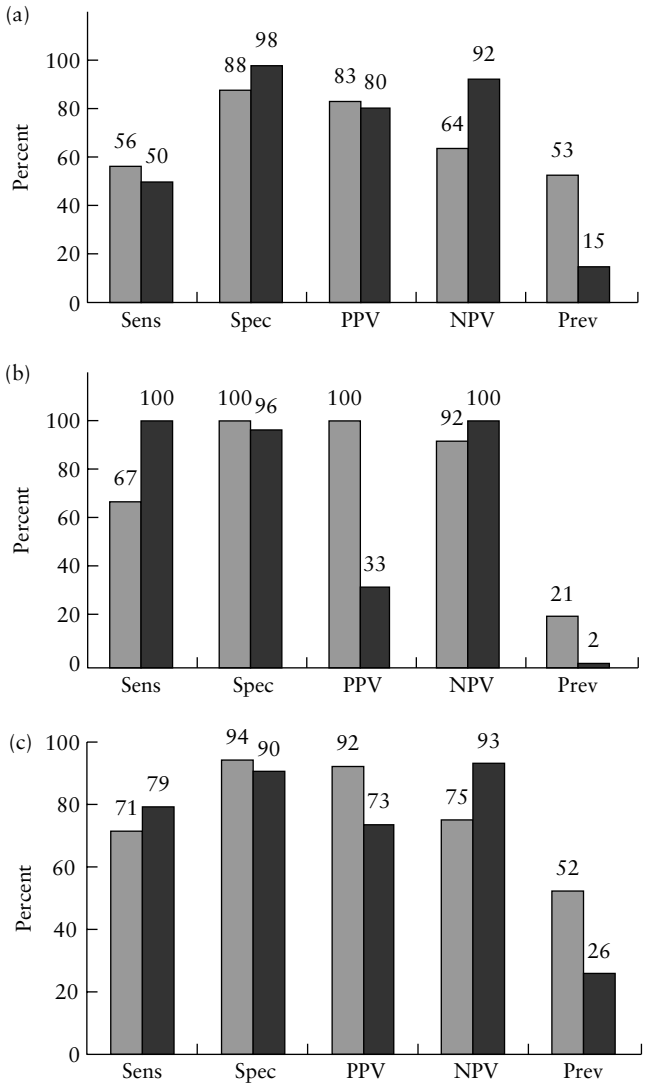

Figure 2 Sensitivity (Sens), specificity (Spec) and positive (PPV) and negative (NPV) predictive values of fetal echocardiography for three specific cardiac segments: (a) systemic venous return, (b) pulmonary venous return and (c) aortic arch differences between 'old' (1998–2000; ▭) and 'new' (2001–2003; ■) cohorts. Prevalence (Prev) of abnormalities in each segment group is also demonstrated.

accordance with the currently published American Society of Echocardiography guidelines regarding imaging of the fetal aortic arch[9]. Finally, although the positive predictive value for the difficult segments was lower in the new cohort, this was probably a result of the significantly lower pre-test probability of lesions (or prevalence of disease) in the newer cohort for those segments, in accordance with Bayes's Theorem. This theorem states that the positive predictive value of a test is dependent on the prevalence of the disease, so that a low prevalence is associated with a higher false-positive rate. Since the prevalence of lesions in these segments dropped (for example, pulmonary venous anomalies occurred with a prevalence of 21% in the old cohort, but only 2% in the new cohort), the positive predictive value also dropped, even though sensitivity and specificity were excellent (100% and 96%, respectively).

This study had some limitations. The problem of verification bias is usually unavoidable in situations where the reference standard (in this case, TTE) is performed as a result of a test (fetal echo). For example, the fetal echos read as normal are not typically verified by postnatal echo. However, since this study assessed the regions systematically, and congenital heart disease often includes co-existing anatomical abnormalities, often our normal segmental findings (such as normal systemic VR) were confirmed when the reference standard (TTE) was performed to address the other, more specific anatomical abnormalities. Additionally, the echocardiographers in this study were not blinded to the fetal echo reports, and this may have influenced interpretation of the reference standard TTE. Finally, these findings were in the setting of a tertiary pediatric cardiac care center, and therefore may not be applicable universally to all other settings.

CONCLUSION

Advances in ultrasound technology have allowed for imaging of the fetal heart with a high degree of 2D and temporal resolution. Given such excellent equipment, a complete, segmental evaluation of the heart, including systemic and pulmonary VR, detailed intracardiac anatomical assessment, and demonstration of the great vessels and branch pulmonary arteries, is developing into the 'standard of care' in fetal echo[9]. Our data show that even more difficult segments, like the aortic arch[12,13], are generally assessable when fetal echo is performed and interpreted with modern equipment and by experienced personnel. As such, our approach to patients in whom these segments remain visualized inadequately is to assume abnormality until proven otherwise. For example, in a fetal patient whose aortic arch cannot be visualized adequately, we assume that there are arch abnormalities and adjust our pre and/or postnatal management accordingly (such as planning repeat fetal echo or early neonatal cardiac evaluation).

As fetal cardiac care continues to evolve from an exclusive diagnostic realm into an interventional modality, it will be imperative not only to describe routinely detailed segment-specific fetal cardiovascular anatomy, but also to assess reliably fetal cardiovascular physiology through available indices of fetal ventricular function and flow. To obtain reliably recently validated indexes, such as pulmonary venous Doppler velocimetry ratios (demonstrated to be potential markers of atrial septal restriction in fetal transposition of the great vessels and hypoplastic left heart syndrome), accurate and reliable imaging of segment-specific fetal cardiac anatomy is essential.

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