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Fetal Echocardiography: Diagnosis of Fetal Cardiac Disease and Utility in Early Neonatal Management

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Disclosures

I have no financial disclosures or conflicts of interest related to the subject matter in this presentation.

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Background

- Incidence of congenital heart disease (CHD) is 5-9 per 1000 live births
- 25% suffer from critical CHD
- CHDs are the most common malformations and the leading cause of death due to malformation in the first year of life
- Prenatal diagnosis of CHD has potential to improve management and outcome
- Fetal echocardiography was initially introduced in the early 1970's and the technology and applications have significantly advanced in the subsequent decades

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Objectives

- To discuss the diagnostic accuracy and limitations of fetal echocardiography in the current era
- Review the guidelines for indications for obtaining a fetal echocardiogram
- To discuss the benefits and limitations of utilizing fetal echocardiography in guiding management during the pregnancy and in the neonatal period

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What Is Included in a Fetal Echocardiogram?

- Cardiac size/axis/position
- Visceral and atrial situs
- AV/VA connections
- Systemic and pulmonary anatomy
- Atrial size
- Atrial septal morphology
- Tricuspid/mitral morphology and size
- Ventricular morphology and size
- Ventricular septal morphology
- Aortic/pulmonary morphology/size
- Great artery relationship/size
- Aortic/ductal arch morphology/size
- Aortic/ductal relationship to trachea
- Proximal branch pulmonary arteries
- MPA/Ascending aortic size
- Assessment for effusions/hydrops
- Heart rate/rhythm/AV conduction
- Color flow and pulsed Doppler assessment of inflows/outflows/arches/pulmonary veins/DV/umbilical vessels
- Color Doppler of atrial and ventricular septa
- Qualitative assessment of ventricular function and wall thickness

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GUIDELINES AND STANDARDS

Guidelines and Recommendations for Performance of the Fetal Echocardiogram: An Update from the American Society of Echocardiography

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Keywords: Prenatal diagnosis, Congenital heart disease, Fetal arrhythmia, Hydrops, Cardiomyopathy

Moon-Grady, Anita J., et al. "Guidelines and Recommendations for Performance of the Fetal Echocardiogram: An Update from the American Society of Echocardiography." Journal of the American Society of Echocardiography (2023).

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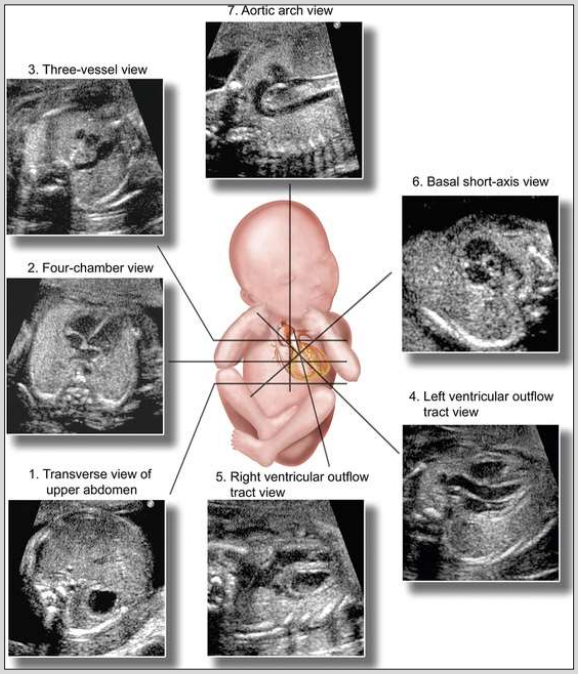

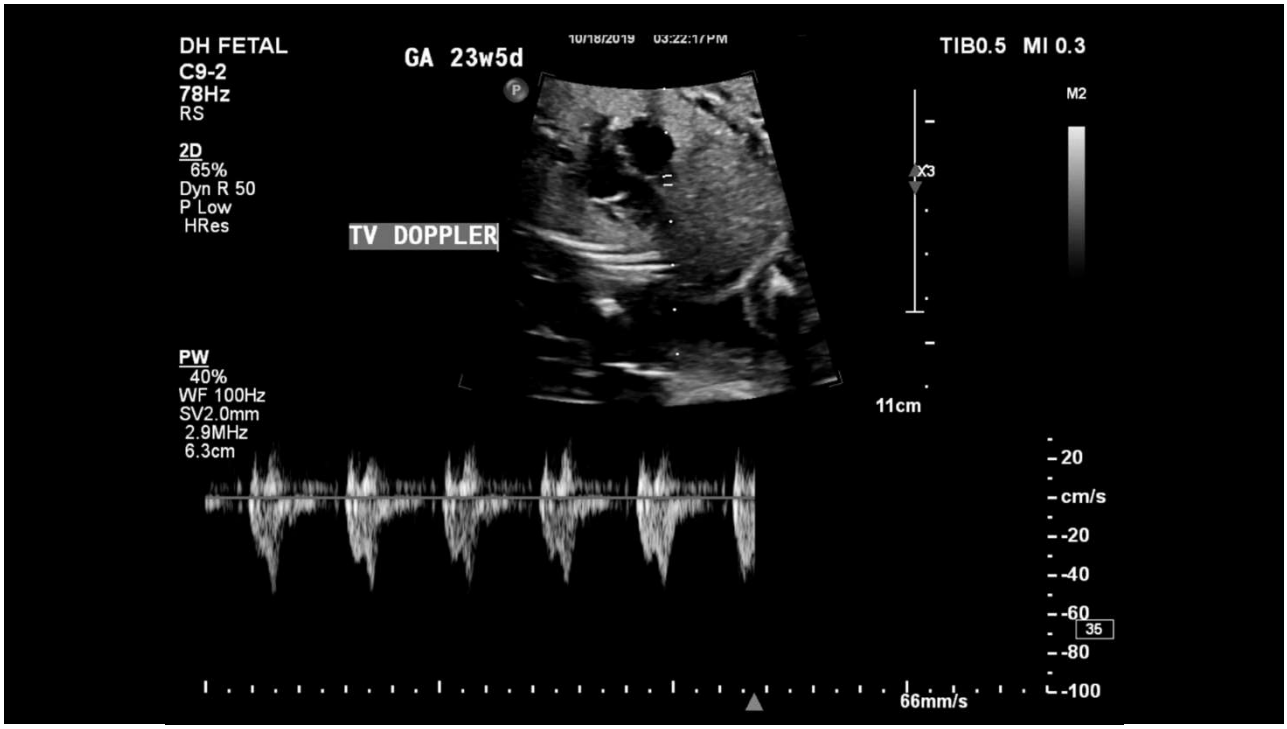

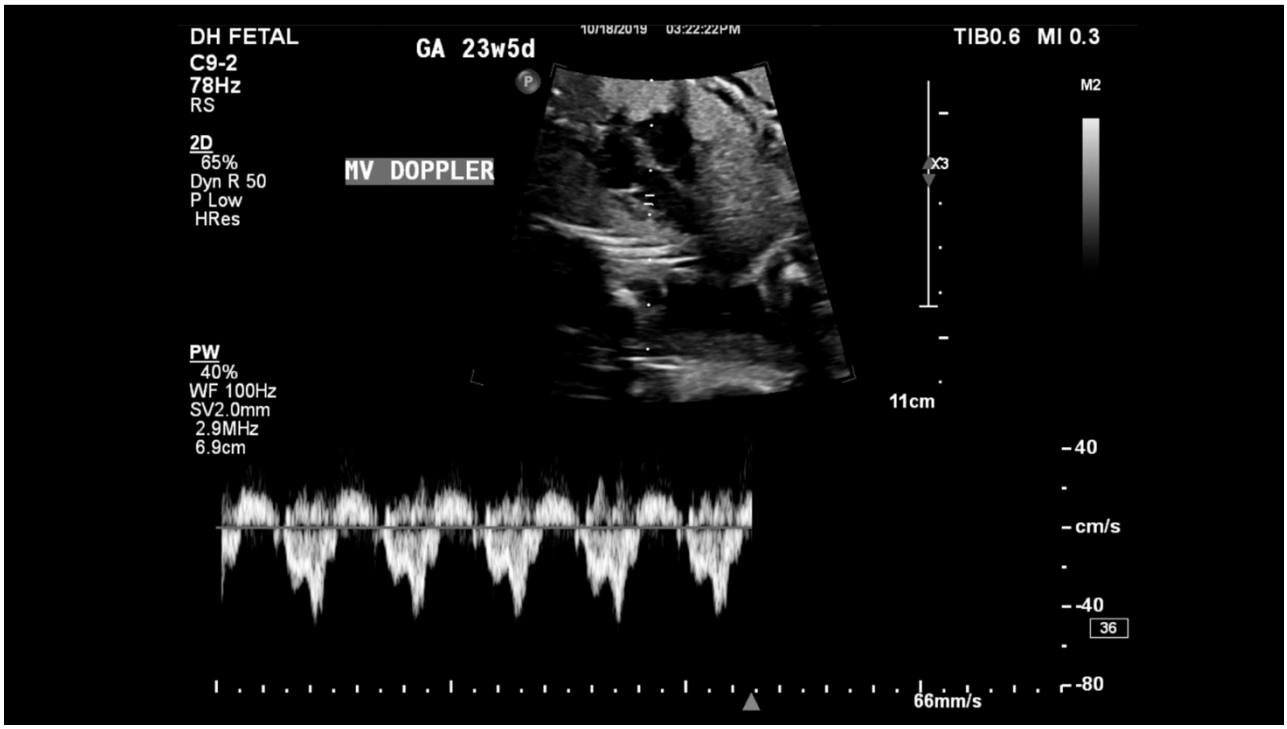
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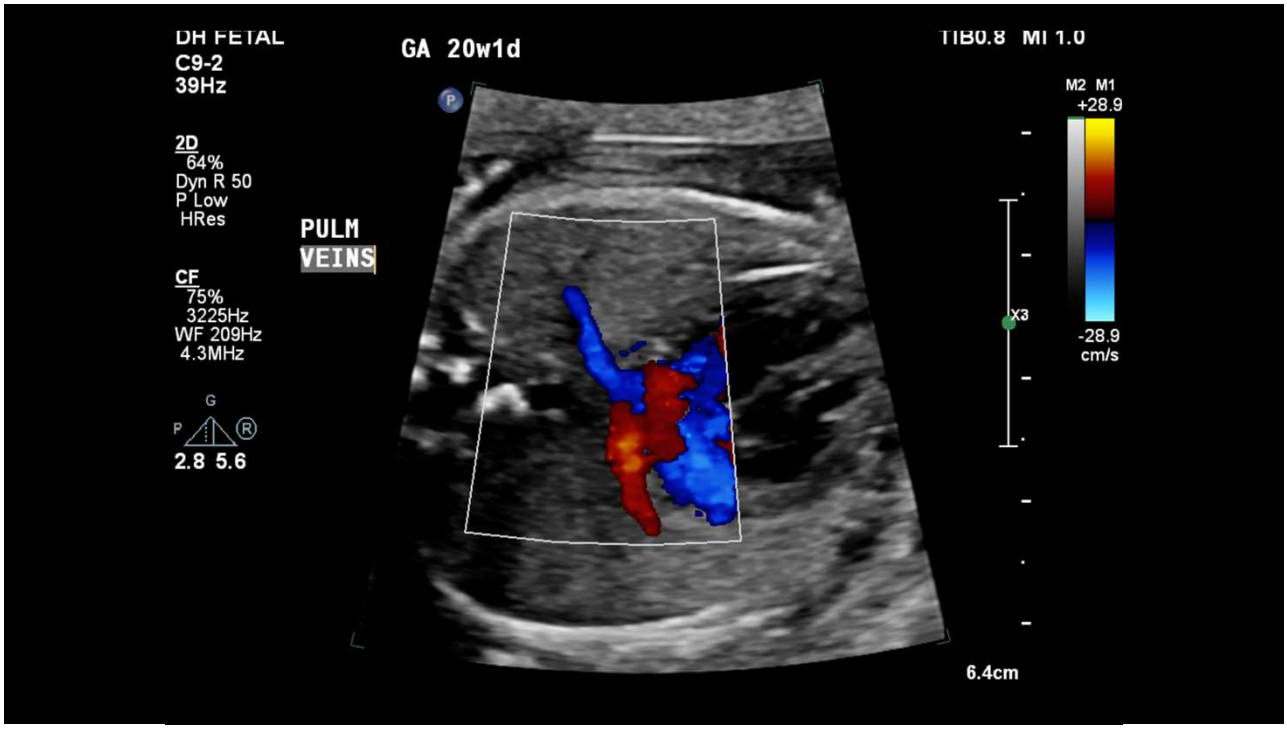
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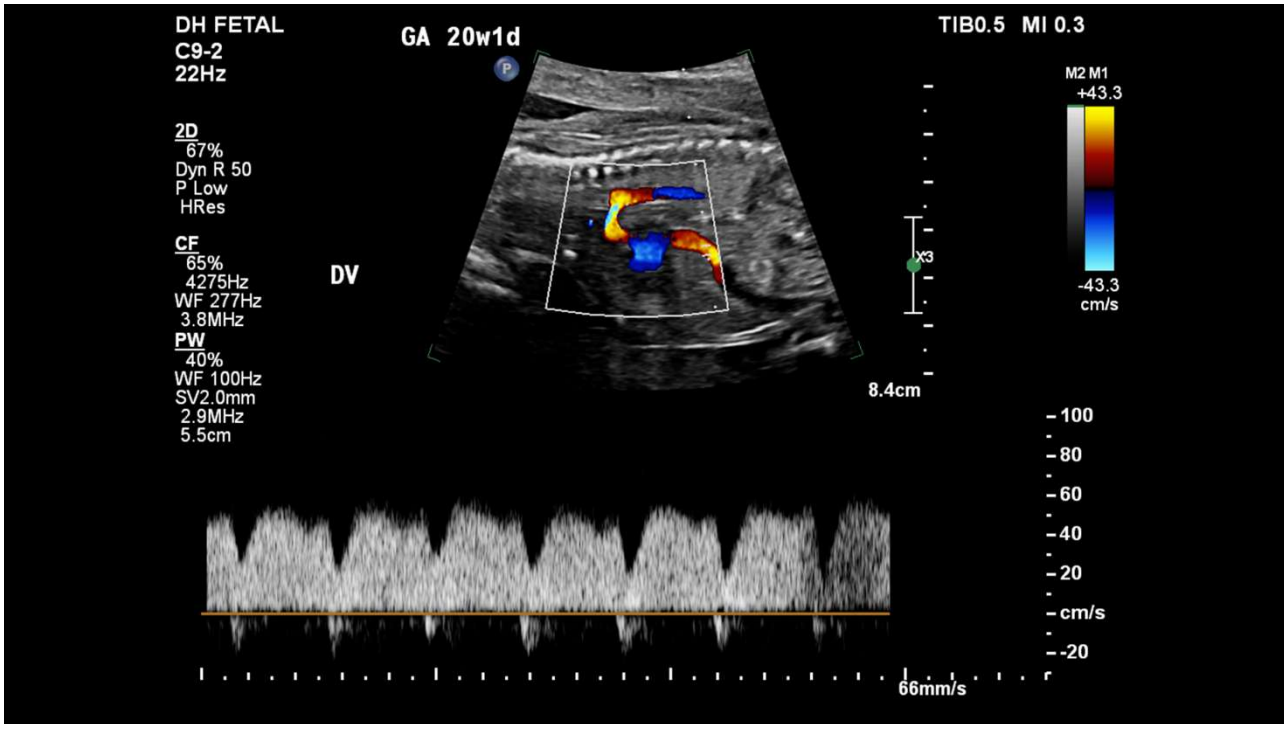
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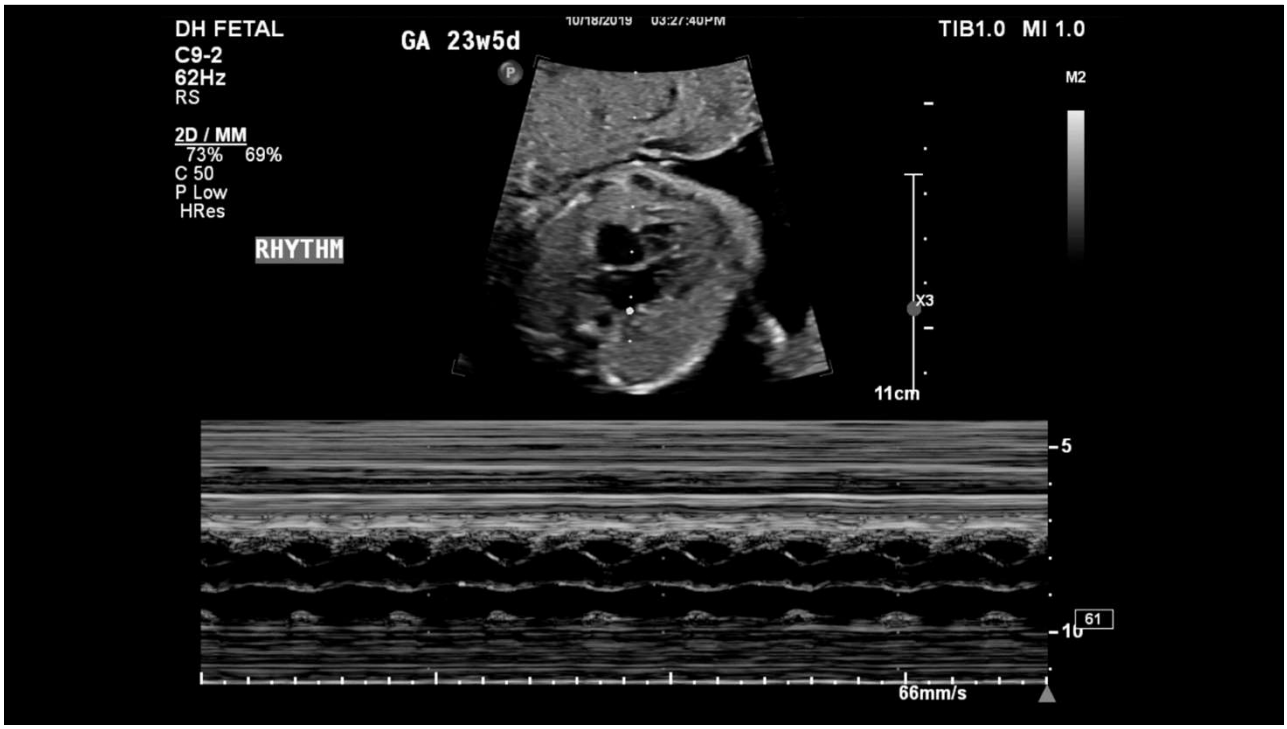

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Accuracy of Fetal Echo

- Accuracy depends on clinical risk of the population, the device capabilities, comprehensiveness of the protocol and the expertise of the operator.
- Hornberger et al. (2022) evaluated accuracy in a single institution from 2007-2018 and reported 90% accuracy
- **Diagnostic accuracy of fetal echocardiography in the 2nd trimester for major CHD is high**
- **Reporting of discrepancies is not well defined**
- Stern et al. (2020) evaluated over 17,000 fetal echocardiograms and found a discrepancy rate of 13.5% for major CHD, mostly minor/moderate in severity and potentially preventable (90%)

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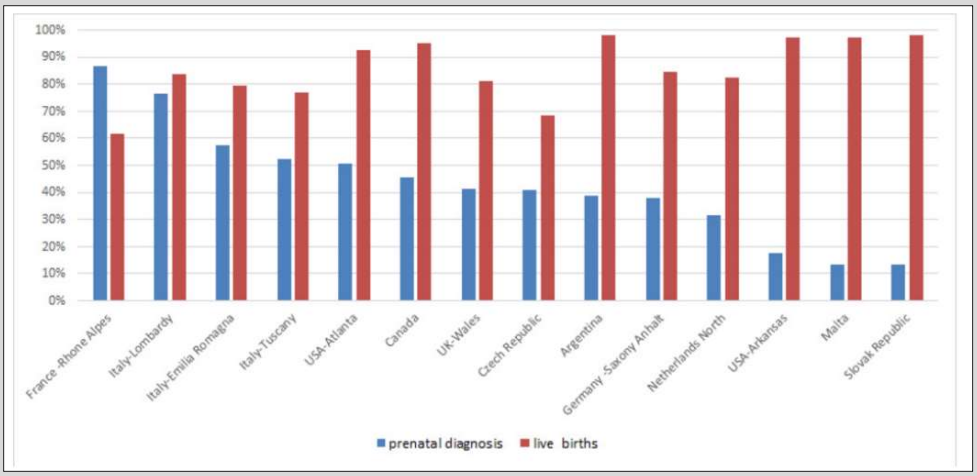
First Trimester Fetal Echo

- Optimal timing for a fetal echocardiogram is 18-22 weeks gestation, but early fetal echocardiography (<16 weeks) gestation is being increasingly performed for high risk cases
- Meta-analysis (2019) of first trimester fetal echocardiography reported a sensitivity of 0.75 and specificity of 0.99
- First trimester fetal echocardiography can miss major forms of CHD, particularly those which progress or evolve later in gestation and repeat should be performed in second trimester



Proportion prenatally diagnosed and proportion of live births among all CCHD cases by programme, International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR) Critical Congenital Heart Defects (CCHD) Prenatal Diagnosis study 2000–2014.

Bakker, Marian K., et al. "Prenatal diagnosis and prevalence of critical congenital heart defects: an international retrospective cohort study." BMJ open 9.7 (2019): e028139.

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Prenatal Detection of CHD

- Reported prenatal detection rates in the community are disappointing
- Quartermain et al. analyzed over 31,000 patients requiring surgical intervention for CHD at age ≤ six months prior to 2013 at 91 US centers through the congenital heart surgical database and found only a 34% detection rate with range between states of 12-53%.
- Davtyan et al. (2023) reported a 58% prenatal detection rate of critical CHD from 2016-2019 at UC San Diego
- Contributing factors to low rates of prenatal detection not clear but may include lack of sonographer/physician training, screening not performed according to guidelines, lack of access, socioeconomic status, and lack of referral for fetal echocardiogram when indicated

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Key Points

- **Despite a high rate of accuracy of fetal echocardiography, prenatal detection rates for CHD remain disappointing.**
- **Need for improved accuracy of screening ultrasounds and expansion of the availability of fetal echocardiography services**
- **Screening may be improved with sonographer/provider education, maintaining a high index of suspicion during screening ultrasounds, adherence to best practice guidelines, and implementing regional and local program assessment using quality improvement metrics**
- **Future of artificial intelligence to detect CHD?…to be determined**

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Limitations of Fetal Echo

Limited Views

Gestational age
Maternal obesity
Fetal position
Fetal motion
Oligohydramnios
Uterine anomalies
Multiples gestation

Hard to Detect

Septal defects
Pulmonary vein anomalies
Coarctation of the aorta
Coronary artery anomalies
Bicuspid aortic valve
Pulmonary arteries
Mild valve anomalies

Lesions Progress/Persist

PDA/PFO
Valve anomalies
Aortic stenosis (HLHS)
Tumors
Cardiomyopathies
Marfan Syndrome
Arrhythmias
Long QT syndrome

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Key Points

- **Always maintain a high index of suspicion for congenital heart disease regardless of the fetal echocardiogram result**
- **Children with a genetic condition that has a high incidence of CHD (Trisomy 21, Turner Syndrome, 22q11 deletion, etc.) should always have a postnatal echocardiogram, even if the fetal echocardiogram is normal**

Fetal Echocardiogram Is Indicated	Absolute Risk	COR/LOE
Pre-gestational diabetes	3-5%	I/A
Uncontrolled PKU	12-14%	I/A
SSA/SSB with (without) previously affected child	11-19% (1-5%)	I/B (IIa/B)
Use of retinoic acid	8-20%	I/B
NSAID use in 3rd trimester	5-50%	I/A
Maternal rubella in 1st trimester	1-2%	I/C
Maternal infection w/ fetal myocarditis	1-2%	I/C
1st degree relative with CHD	Mom 3-7%, Dad 2-3%, Sibling 3%	I/B
1st/2nd degree relative with disease of Mendelian inheritance associated with CHD (i.e., 22q11, William's Syndrome)	Up to 50%	I/C
Suspected CHD on screening ultrasound	40%	I/B
Extracardiac anomaly on screening ultrasound	20-45%	I/B
Fetal chromosomal anomaly	Up to 90%	I/C
Fetal arrhythmia/tachycardia/bradycardia	2% / 1% / 50%	I/C
NT > 3.5 mm or > 3 mm with abnormal DV flow	6-60%	I/A
Monochorionic twins	2-10%	I/A
Hydrops fetalis or pleural/pericardial effusion	15-25%	I/B

Fetal Echocardiogram May Be Considered	Absolute Risk	COR/LOE
Maternal use of vitamin A in first trimester	1.8%	IIb/B
First trimester SSRI use (paroxetine only)	1-2%	IIb/A
NSAID use in the first trimester	1-2%	IIb/B
Abnormal umbilical cord/placenta/abdominal vein	3.9%	IIb/C
Assisted reproductive technology	1.1-3.3%	IIa/A
Increased NT of 3-3.4 mm	~3%	IIa/A
Maternal use of ACE-I in 1st trimester	2.9%	IIa/B

Fetal Echocardiogram Is NOT Indicated	Absolute Risk	COR/LOE
Gestational diabetes mellitus with HbA1c < 6%	<1%	III/B
Maternal use of anticonvulsants in first trimester	1.8%	IIb/A
Maternal use of lithium in the first trimester	<2%	IIb/B
Congenital heart disease in a 2nd degree relative	<2%	IIb/B
Maternal use of SSRI's other than paroxetine	<1%	III/A
Maternal use of vitamin K agonists (Coumadin)	<1%	III/B
Maternal infection (other than rubella) with seroconversion only	1%	III/C
Isolated CHD in relative other than 1st or 2nd degree	`1%	III/C
Obesity (BMI > 30 kg/m2)	1-2%	III
Isolated single umbilical artery	1.2-1.8%	III

Donofrio, Mary T., et al. "Diagnosis and treatment of fetal cardiac disease: a scientific statement from the American Heart Association." Circulation 129.21 (2014): 2183-2242.

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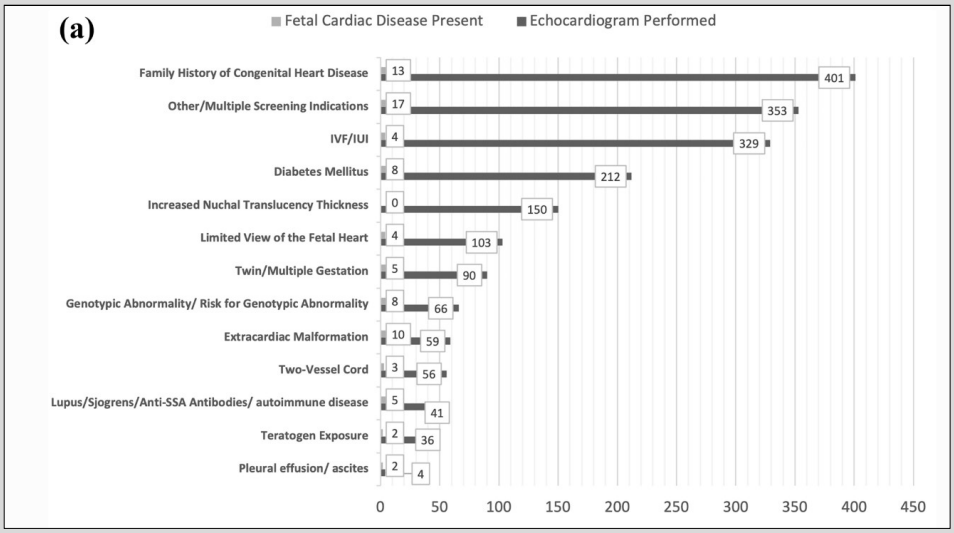

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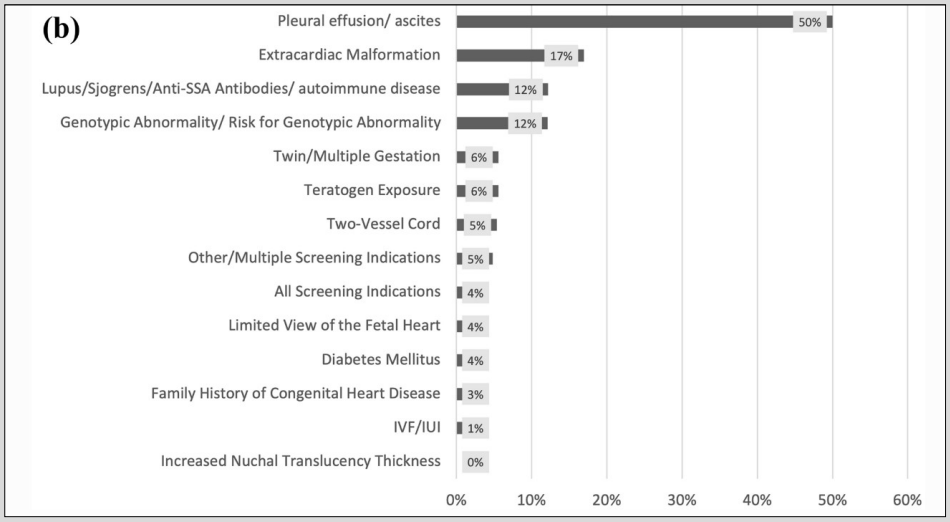

Prevalence of fetal CHD for each screening indication

Makkar, Nupur, et al. "Prenatal Detection of Congenital Heart Disease: Importance of Fetal Echocardiography Following Normal Fetal Cardiac Screening." Pediatric Cardiology (2022): 1-8.

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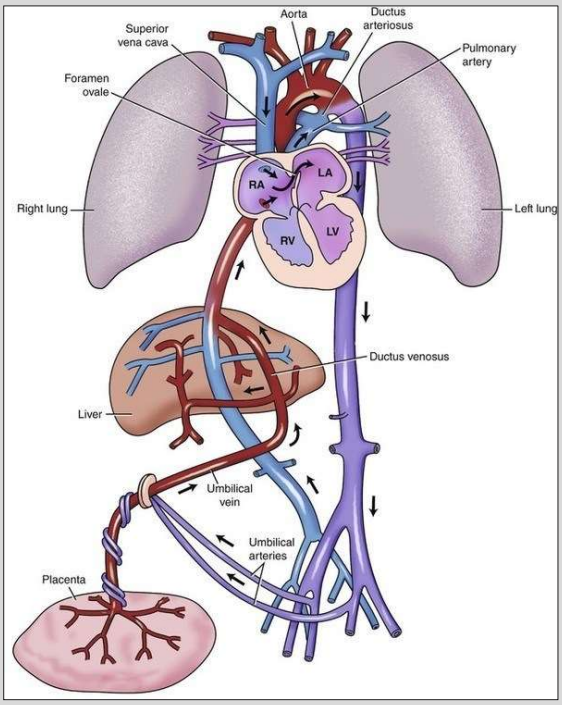
Key Points

- **With improvements in screening ultrasounds, there is diminishing utility of fetal echocardiography to detect major forms of CHD following normal fetal cardiac screening.**
- **The necessity of a fetal echocardiogram for indications that carry a risk of 2-3 % is controversial.**
- **Availability of local resources, healthcare system environment, and skill of screening operators should be considered.**
- **A fetal echocardiogram is always indicated when views of the heart appear abnormal, regardless of other risk factors.**



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Published Benefits of Fetal Echo

- Kumar et al. found improvements in pre-operative status for patients with d-TGA and HLHS, but no improvement in pre-operative mortality or early post-operative outcome
- Tworetzky et al found significant improvement in peri-operative status and survival in HLHS
- Bonnet et al found a significant decrease in neonatal mortality and morbidity when d-TGA is prenatally diagnosed and appropriately managed
- Holland et al found reduced mortality prior to planned cardiac surgery with prenatal diagnosis
- Peyvandi et al conducted MRIs and found lower brain injury and better brain development in those prenatally diagnosed
- Morris et al and Eckersley et al reported higher neonatal mortality in CCHD patients delivered remote from a cardiac surgical center

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Benefits of Fetal Echo

- Impact on morbidity:
  - Infants with ductal dependent lesions may be less hemodynamically compromised in pre-operative period
  - Fewer neurological sequelae in infants with HLHS
  - May reduce hospital length of stay for biventricular repair
- Impact on survival:
  - Sparse data- some suggest improved survival for d-TGA/HLHS
  - May decrease mortality by minimizing delay in those needing emergent intervention
- May reduce in hospital cardiac care cost
- Allows for in-utero treatment
  - Incessant fetal tachyarrhythmias
  - Fetal auto-immune mediated myocardial disease (IVIG/steroids)
  - Fetal intervention (rare)

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Benefits of Fetal Echo During Pregnancy

- Permits appropriate parental counseling and parental decision making
- Facilitate multidisciplinary consultations including genetic counseling
- Evaluation for extracardiac anomalies
- Consider additional imaging (MRI for brain and pulmonary development)
- Prediction of the clinical course and plan for follow up
  - Repeat fetal cardiac and MFM visits to evaluate for progression and complications
  - Fetal wellness assessments in 3rd trimester (kick counts, NSTs, and BPPs) for fetuses at risk for hypoxemia and acidosis
- Screening for and addressing parental stress: social services, counseling, child life
- In utero treatment (arrhythmias, aortic stenosis, HLHS)

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Use of Fetal Echo During Delivery

- Planning for delivery location
- Individualized and specialized delivery planning and perinatal management
- Team preparation
- Prepare for management in the delivery room which depends on:
  - Risk of hemodynamic instability anticipated at birth
  - Medical resources available in the region
  - Distance to the cardiac care center
  - Type and availability of the transportation to the cardiac center
  - Anticipated or known obstetric or maternal complications.

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Risk Stratification/Care Optimization

- Planned delivery: typically at 39 weeks by IOL
- Coordination of services: neonatology, cardiology, cardiac surgery, obstetrics, pulmonary
- Allows for disease specific care in the delivery room (guidelines available)
- Initiation of PGE for ductal dependent lesions
- Prepare for balloon atrial septostomy in at risk patients
- Prepare for ECMO in infants at risk for rapid respiratory decompensation: Ebstein anomaly/TOF with absent pulmonary valve
- Incessant tachyarrhythmias:
  - Close monitoring for heart failure and fetal distress
  - Medical and electrical cardioversion available
- Pacing for infants with complete heart block

Table 1 Definition of LOC assignment and coordinated action plan

LOC	Definition	Example CHD	Prenatal planning	Delivery	DR recommendations
1	CHD without physiologic instability in first weeks of life	1. Shunt lesions (e.g., ASD, VSD, AVSD) 2. Benign arrhythmias	Arrange outpatient cardiology evaluation	Spontaneous vaginal delivery	Routine DR management
2	CHD with physiologic stability in DR but requiring postnatal intervention/surgery before discharge	1. Ductal-dependent lesions or lesions with complex physiology likely to require neonatal intervention/surgery (e.g., HLHS, PA/IVS, truncus arteriosus) 2. Nonsustained or controlled tachyarrhythmias	Create plan of care for DR stabilization and neonatal management by local hospital with transport to CNMC	Spontaneous vaginal delivery vs induction near term	Neonatologist in DR; initiate PGE at low dose for ductal-dependent lesions
3	CHD with expected instability requiring immediate specialty care in DR before anticipated stabilizing intervention/surgery	1. HLHS/RFO 2. D-TGA/RFO 3. Severe Ebstein's anomaly with dilated right ventricle and low RV pressure 4. TOF/APV with RV and/or LV dysfunction and cardiac shift 5. Sustained tachyarrhythmias or CHB with heart failure	Create plan of care to include specialized CNMC team in DR and interventional/ surgical team on standby	Planned induction usually at 39 wk with "bailout" C/S if necessary for care coordination	Neonatologist and CNMC specialists in DR; stabilizing medications predetermined by care plan
4	CHD with expected instability requiring immediate specialty care and urgent intervention/surgery in DR to improve chance of survival	1. HLHS/IAS 2. D-TGA/severe RFO or IAS with abnormal DA flow 3. Severe Ebstein's anomaly or TOF/APV with hydrops 4. Tachyarrhythmias/ bradyarrhythmias with hydrops	Create multidisciplinary plan of care to include CNMC delivery if possible with specialized care team in DR and interventional/ surgical team ready	Planned C/S at CNMC usually at 38–39 wk or sooner if there is evidence of fetal distress or hydrops Maternal risk determined by obstetrician (only low-risk women deliver at CNMC)	Specialized care team in DR Stabilizing medications/ equipment predetermined by care plan

Donofrio, Mary T., et al. "Risk-stratified postnatal care of newborns with congenital heart disease determined by fetal echocardiography." Journal of the American Society of Echocardiography 28.11 (2015): 1339-1349.

CHD diagnosis	Fetal echocardiogram findings	Delivery room (DR) recommendations
ASD, VSD or AVSD (shunt lesions); Mild valve abnormalities	Isolated ASD or VSD with normal FO and DA flow, normal or minimal flow disturbances at valves, and normal heart function (LOC 1)	Routine care, hospital or telemedicine consult Outpatient cardiology follow-up
Coarctation, critical (ductal dependent lesion)	Ductal dependent coarctation (LOC 2): 1. Left/right heart size discrepancy with MV/TV and AoV/ PV ratios <0.6[52] 2. Distal arch in 3rd trimester <3 mm [52] 3. AoI/DA in 3VV <0.75[53] 4. Abnormal Doppler flow in isthmus[13,54] 5. Posterior shelf[56]	Initiation of prostaglandin infusion through peripheral IV or umbilical line Intubation with mechanical ventilation only if clinically indicated Transfer to cardiac center
Pulmonary atresia, HLHS, other single ventricles, or cyanotic TOF (ductal dependent lesions)	Ductal dependent pulmonary circulation (LOC 2): 1. Aorta to pulmonary flow in the DA[37,38] 2. Reversed orientation of the DA (inferior angle <90°) [39] 3. Pulmonary valve z-score value less than 3, after 16 weeks[40] Ductal dependent systemic circulation (LOC 2): 1. Left to right atrial flow across the foramen ovale and distal aortic arch[37,41]	Initiation of prostaglandin infusion through peripheral IV or umbilical line Intubation with mechanical ventilation only if clinically indicated Transfer to cardiac center
HLHS and variants with severely restrictive or intact atrial septum	Pulmonary vein Doppler[42,43]: 1. Moderate obstruction: PV f/r <5 and >3 (LOC 3) 2. Severe obstruction: PV f/r <3; (LOC 4)	Initiation of prostaglandin infusion through peripheral IV or umbilical line Intubation with mechanical ventilation OR or cath lab on standby Plan for immediate intervention to decompress left atrium ECMO available

TAPVR Obstructed	Pulmonary vein Doppler[50]: 1. Monophasic nonpulsatile pulmonary (LOC 4) 2. Infradiaphragmatic TAPVR (LOC 3 or 4)	Intubation with mechanical ventilation Peripheral IV and/or umbilical line OR team on standby Initiation of prostaglandin infusion (may relax the ductus venosus smooth muscle for infradiaphragmatic TAPVR) Plan for immediate surgical intervention
D-TGA and variants with restrictive atrial septum	Foramen ovale findings[45,46]: 1. Hypermobile septum (LOC 3) 2. Angle of septum primum <30° (LOC 3) 3. Lack of swinging motion of septum or "tethered" septum (LOC 3) 4. Bowing of atrial septum >50% (LOC 3 or 4) 5. intact (LOC 4) Abnormal ductus arteriosus[47-48]: 1. With additional RFO (LOC 4) 2. Small with moderate/severe restriction (LOC 3 or 4) 3. Reversed, bidirectional or accelerated flow (LOC 3 or 4) Pulmonary vein Doppler, proximal to the left atrium[49]: 1. Max velocity "s" wave >41 cm/s (LOC 3 or 4)	Initiation of prostaglandin infusion through peripheral IV or umbilical line Intubation with mechanical ventilation Cath lab on standby Plan for immediate balloon atrial septostomy If ductal flow abnormal, consider pulmonary hypertension therapy including intubation, 100% oxygen, inhaled nitric oxide
TOF/APV	1. With associated cardiac dysfunction (LOC 3) 2. With associated hydrops fetalis (LOC 4) 3. Lung findings suggestive of compression or fluid trapping (LOC 4)	Specialized cardiac care team in the DR Specialized ventilation (prone) Peripheral IV or umbilical access Intubation with mechanical ventilation if needed Consider 100% oxygen and inhaled nitric oxide to decrease pulmonary resistance Consider ECMO

CHD diagnosis	Fetal echocardiogram findings	Delivery room (DR) recommendations
Severe Ebstein's anomaly	1. With associated cardiac dysfunction (LOC 3) 2. With associated hydrops fetalis (LOC 4)	Specialized cardiac care team in the DR Specialized ventilation (prone) Peripheral IV or umbilical access Intubation with mechanical ventilation if needed Consider 100% oxygen and inhaled nitric oxide to decrease pulmonary resistance Consider ECMO cardioversion or medical therapy in DR as indicated for arrhythmia
Unstable tachyarrhythmias	1. With associated heart failure (LOC 3) 2. With associated hydrops fetalis (LOC 4)	Consider early delivery if gestational age appropriate Cardioversion and/or medical therapy in DR
Complete heart block with low ventricular rate and/ or cardiac dysfunction	1. With associated heart failure (LOC 3) 2. With associated hydrops fetalis (LOC 4)	Consider early delivery if gestational age appropriate Consider chronotropic agents vs. temporary pacing in DR

Sanapo, Laura, et al. "Fetal echocardiography for planning perinatal and delivery room care of neonates with congenital heart disease." Echocardiography 34.12 (2017): 1804-1821.

	# of fetuses with f/u	Actual LOC 1: # with postnatal outpatient follow-up	Actual LOC 2: # with postnatal transfer for surgery or intervention	Actual LOC 3: # requiring postnatal urgent stabilizing intervention	Actual LOC 4: # requiring postnatal emergent stabilizing intervention
Prenatal LOC 1: CHD expected to be stable in 1st weeks of life though outpatient f/u needed	195	193	2	0	0
Prenatal LOC 2: CHD expected to be stable in DR though surgery/cath required	229	22	200	6	1
Prenatal LOC 3: CHD with risk of compromise in DR; Team on standby	20	0	3	6	11
Prenatal LOC 4: CHD expected to be compromised in DR; Team ready	19	0	2	1	16

Donofrio, Mary T., et al. "Risk-stratified postnatal care of newborns with congenital heart disease determined by fetal echocardiography." Journal of the American Society of Echocardiography 28.11 (2015): 1339-1349.

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Key Points

- Outcomes for infants with CCHD are best when disease is recognized prenatally and promptly managed in an appropriate facility with disease specific optimized care
- Risk stratification and care optimization may not only improve outcomes, but also reduce cost of care
- More research is still needed to determine optimal care and the benefits of these strategies, especially for certain lesions (i.e. coarctation of the aorta, d-TGA)

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Conclusion

- Fetal echocardiography accurately diagnoses CHD and can be used to predict the postnatal severity of the disease and guide postnatal care.
- However, prenatal detection rates of CHD in the community remain low so improved detection by prenatal screening is needed.
- Fetal echocardiography still has some limitations in achieving an accurate diagnosis and in predicting outcome, especially for certain conditions.
- Optimal management and delivery of infants diagnosed with CHD includes using features on the fetal echocardiogram to risk stratify and provide guidance for disease specific postnatal management.

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