

Early Fetal Echocardiography at the Time of 11⁺⁰–13⁺⁶ Weeks Scan

¹Marcin Wiechec, ²Agnieszka Nocun, ³Jill Beithon RT

¹IPL Medical Practice Marcin Wiechec, Krakow, Poland

²IPL Medical Practice Agnieszka Nocun, Krakow, Poland

³Merit Care Health System, Fargo, ND, USA

Correspondence: Marcin Wiechec, IPL Medical Practice Marcin Wiechec, 3 Szczepanski Place, 30-011 Krakow, Poland
Phone: +48602594710, e-mail: marcin74@mp.pl

Abstract

Early Fetal Echocardiography (EFE) is generally defined as a fetal cardiac scan performed until 16 weeks of gestation. Fetal indications for EFE in the first trimester are in strong connection with ultrasound findings during routine nuchal scan: early diagnosed extracardiac malformations, abnormal ductus venosus (DV) velocimetry, tricuspid valve regurgitation (TR), single umbilical artery and increased NT measurement as a major fetal factor. Essential components of EFE include: abdominal view (AbdV), four chamber view (4CV), three vessel view (3VV), origin and cross-over of the great arteries (GA), aortic arch (AoA), ductal arch (DA), superior and inferior venae cavae and at least 2 pulmonary veins.

EFE has some limitations, which determine delayed diagnosis of some CHDs. Early fetal echocardiography is feasible and reasonable. It gives parents the opportunity to exclude approximately 60% of cardiac abnormalities and to reassure them of normal heart anatomy as early as possible.

Keywords: Early fetal echocardiography, early prenatal diagnosis, first trimester, congenital heart defects.

INTRODUCTION

Early Fetal Echocardiography (EFE) is generally defined as a fetal cardiac scan performed until 16 weeks of gestation. It is recognized as a highly specialistic scan under exceptional indications, including: increased nuchal translucency (NT) measurement; congenital heart defect (CHD) risk factors, early diagnosed extracardiac fetal abnormalities.^{1,2} This selective approach produces limited CHD detection rate using mainly NT cut-offs.³⁻⁵ Therefore it is rather indicated to perform EFE as a routine part of every early routine ultrasound fetal assessment, which in most of the countries interferes with nuchal scan between 11⁺⁰–13⁺⁶. This approach increases detection rate of CHDs in the first trimester to nearly 60-80%.^{3,6} Additional reasons to perform EFE at the nuchal scan are: CHDs are the commonest anomalies (approx 33% of all structural abnormalities), they are connected with aneuploidies and genetic syndromes, early diagnosis means early decision making, anatomical relations between cardiac structures at 11⁺⁰–13⁺⁶ weeks are very similar as in the second trimester and finally contemporary ultrasound equipment makes EFE easier.⁸⁻¹¹ It is important to emphasize, that the severest CHDs do not develop from normal looking heart and demonstrate similarly

abnormal views in the first, second and third trimester. Among them d-transposition of great arteries (d-TGA), l-transposition of great arteries (l-TGA), hypoplastic left heart syndrome (HLHS) based on aortic and mitral atresia or severe stenosis, atrioventricular septal defect (AVSD), double outlet right ventricle (DORV), common arterial trunk (CAT), double inlet left ventricle (DILV), tricuspid atresia (TA), mitral atresia (MA), pulmonary atresia (PA), heterotaxy syndromes, total anomalous pulmonary venous return (TAPVR), large ventricular septal defects (VSD) are distinguished.⁹

INDICATIONS

In general indications for fetal echocardiography are divided into maternal and fetal.¹² Maternal factors are the same for early and mid-gestational fetal echocardiography. Fetal indications in the first trimester are in strong connection with ultrasound findings during routine nuchal scan: early diagnosed extracardiac malformations, abnormal ductus venosus (DV) velocimetry, tricuspid valve regurgitation (TR), single umbilical artery and increased NT measurement as a major fetal factor. Thickening of NT is markedly associated with increased risk of CHD and namely increases

from about 0.5% in fetuses with NT < median; 1% for NT between median and 95th percentile, 2% for NT between 95th and 99th percentile and to 3.5%; 6.5%; 12.5% for NT of 3.5-4.4 mm; 4.5-5.4 mm; ≥ 5.5 mm respectively.¹³ There are various policies reported regarding NT cut-off as an indicator for fetal echocardiography ranging between 95th percentile (2.2 mm to 2.8 mm depending on CRL measurements) to 99th percentile equal to 3.5 mm.^{14,15} Detection rates for CHD using 3.5 mm NT cut-off varies significantly from 3.7 to 40%, depending on the published series.^{16,17} Though Hyett and colleagues obtained very good sensitivity basing on NT screening their prevalence of CHDs was low (1.7/1000).¹⁷ Comparably Westin and co-workers reported detection rate at the level 5.8% with markedly higher CHD prevalence of 3.3/1000 basing on low-risk population.⁴ As a response some authors suggested to decrease NT cut-off to 95th percentile to improve sensitivity however at the end it resulted in strongly increased false positive rate and unnecessary referrals to tertiary centers.¹⁴ Hafner et al same as Makrydimas and co-workers concluded in their studies association between increased NT and CHD in the setting of aneuploidy or extracardiac malformations.^{15,16} Moreover Maiz et al proved that risk of CHD based on NT measurement differs depending on co-existence of reverse or positive a-wave in DV velocimetry and it was three fold higher or two fold lower respectively.¹³ Favre et al. examined euploid fetuses with diagnosed CHDs and increased NT measurements with coexisting abnormal ductus venosus velocimetry. Ninety percent sensitivity was achieved (10 CHDs, 9 increased NT measurements together with abnormal DV flow).¹⁸ Berg and co-workers found association between obstructive lesions of the right heart with intact ventricular septum and hyperdynamic DV velocimetry or even reverse A – wave during atrial contraction.¹⁹

Connection of specific type of cardiac anomalies and increased NT was investigated. Hyett and co-workers¹⁷ and Orvos et al.¹⁴ found a significant association with left heart lesions and septal defects, however, Makrydimas¹⁵ in the multicenter study based on 637 CHDs did not support this hypothesis.

It is important to emphasize, that normal NT measurements below the 95th percentile do not significantly decrease the prevalence of CHDs.⁴ Becker and colleagues divided fetuses with diagnosed CHDs into two groups according to the NT measurement.³ In the group with NT below 2.5 mm 31.4% of major defects were found (atrioventricular

septal defect, hypoplastic right heart syndrome, absent pulmonary valve syndrome, d-transposition of great arteries, tetralogy of fallot, total anomalous pulmonary venous return). To conclude increased NT is a good indicator for fetal echocardiography, however, because of a small number of CHDs connected with increased NT, NT thickening is a poor screening tool for cardiac malformations.

EARLY FETAL ECHOCARDIOGRAPHY REQUIREMENTS

There are several conditions for successful EFE at the time of the nuchal scan. EFE performance is based on combined transabdominal (TA) and transvaginal (TV) accesses using high frequency transducers. There are two possible access strategies: first using transvaginal approach only when transabdominal cardiac views are suboptimal and second using complementarily transabdominal and transvaginal accesses as a routine. In authors opinion the second strategy is more advocated. Afterwards operator dependent skills cannot be disregarded. These are divided into following subcategories: good scanning technique in the detailed first trimester assessment; competence in transvaginal scanning; high expertise in fetal echocardiography and technical efficiency in image optimization. There are some equipment limitations, therefore it is recommended for EFE to use top of the edge ultrasound machines, well-appointed in wide spectrum of modern image enhancers.

IMAGE OPTIMIZATION

The value of image optimization is pronounced when a difficult patient is scanned. In this case standard settings of the ultrasound machine are not sufficient in producing high quality images. Operators who are familiar with optimal probe selection, image enhancers, filters and adjustments for the particular kind of patients demonstrate better ultrasound imaging. This is one of the reasons of operator dependency in medical ultrasound. In the second trimester classical image optimization by correcting gain control and depth of the beam may be rather effective in most of the cases, but for the first trimester this is not enough. In obstetrics the most difficult ultrasound subjects are first trimester fetuses. They require high frequency transducers from transabdominal (i.e. 4-8 MHz) as well as from transvaginal (i.e 5-9 MHz) access. Lombardi et al demonstrated that linear probes with the frequencies of 6 MHz and 15 MHz produce high quality first trimester cardiac

views.²⁰ They used one of these probes depending on the patient's BMI and distance from the fetus to the patient's abdominal wall. In 2006 6-12 MHz transvaginal transducer was introduced, which improved visualization of cardiac anatomy between 11 and 12 weeks of gestation. Regarding the settings von Kaisenberg and co-workers raised that the combination of harmonics and compounding shows good reproducibility and demonstrability of cardiac imaging in the first trimester.²¹ Authors of this review utilize high harmonics, low compounding and high levels of speckle reduction algorithm. Harmonic imaging improves spatial resolution to enable visualization of smaller objects, contrast resolution to demonstrate fine differences in grayscale. Compounding on the other hand enhances even more contrast resolution and allows for better tissue differentiation. It results in visualization of filmy organ borders. By using this modality, crystals within the probe transmit pulses both in perpendicular and oblique directions. Speckle reduction algorithm is one of the newest image enhancers which results in imaging based on speckle suppression, edge enhancement, and feature preservation. Dynamic range control and rejection control should be optimized for the particular patient to produce better contrast imaging, when needed. Because in the first trimester the fetal heart is so small (6 mm-10 mm across), it is crucial to utilize the maximum available high definition zoom box which creates a field of approximately 24 mm × 29 mm in the axial view. This allows for the highest spatial and temporal resolution possible. Color Doppler imaging is recommended and widely used in EFE. When this modality is in operation productivity of the transducer is divided into gray scale imaging and color mapping, what causes the drop-off in frame rate. Operator needs to control color information at the levels of frame rate over 20 because of the fast beating fetal heart in the first trimester. There are basic and advanced controls. Among basic ones color gain corrects sensitivity of color mapping, quality corrects resolution, wall motion filter eliminates vessel wall motion noise and PRF selects velocity range. Advanced filters correct digital appearance of color mapping, transmit frequency, axial resolution, amount of color over bright echoes, temporal averaging of rising and falling velocity, number of pulses, line density, reduction of movement artifacts and lateral filtering.

EFFECTIVENESS AND LIMITATIONS

Formation of the cardiovascular system originates from the mesodermal germ layer and begins at the 22 day of

development, when the embryo is approximately 2.5-3 mm in length. The process is completed at the time of 56 days (8 weeks of development = 23 Carnegie stage), when the embryo is 30 mm in length (9 weeks + 6 days according to Hadlock 92 Tables).²² Referring to these facts fetal heart assessment is theoretically possible at the time of 10 weeks of gestation. Practically ultrasound imaging allows for effective fetal cardiac evaluation starting from 11 weeks. Essential components of EFE include: abdominal view (AbdV), four chamber view (4CV), three vessel view (3VV), origin and cross-over of the great arteries (GA), aortic arch (AoA), ductal arch (DA), superior and inferior venae cavae and at least 2 pulmonary veins. Smercek et al. basing on above criteria showed total success rate in visualization of 45% at 11 weeks and of 90% at 13⁺⁶ weeks.²³ Successful visualization rate of cardiac structures in the first trimester is strongly dependent on the published methodology. Haak and co-workers in 2002, using following criteria: 4CV, GA, 3VV, obtained only 20% at 11 weeks, but 92% at 13 weeks.²⁴ Furthermore Vimpelli et al. achieved 43%, 56% and 62% at 11, 12 and 13 weeks respectively (criteria: 4CV, GA, AoA, DA).²⁵ All these data come from studies where, older generation of ultrasound systems was applied (HDI 5000 Philips Medical Systems equipped with 4-8 MHz TV transducer and 7 MHz TA transducer; Hitachi EUB-6000 equipped with 5-7.5 MHz TV transducer), so far no series were published based on the newest ultrasound scanners.

Several studies were published showing detection rates of CHD at the time of nuchal scan. Details are displayed in Table 1. Some of the examples of cardiac abnormalities detected in the authors material in the first trimester are displayed in Figures 1 to 3C.

EFE has some limitations, which determine delayed diagnosis of some CHDs. In singular cases when transabdominal approach is suboptimal and simultaneously the localization of the fetus is out of the penetration of transvaginal probe, it is time consuming or even unobtainable. It was reported, that several CHDs may be overlooked in the first trimester, like later onset of developmental lesions (coarctation of aorta, mild aortic or pulmonary stenosis, mild tricuspid and mitral valve abnormalities, cardiac tumors, cardiomyopathies); septal defects including ventricular, atrioventricular, primum atrial septal defects; others, like tetralogy of fallot with normal size pulmonary arteries or abnormalities of pulmonary venous return.¹

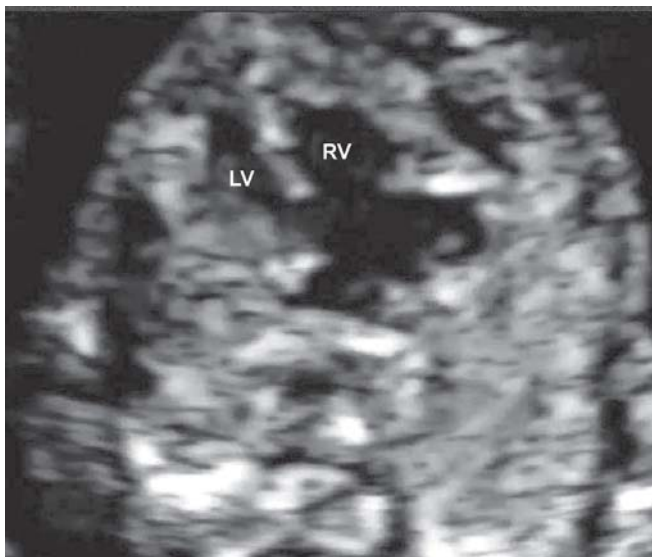
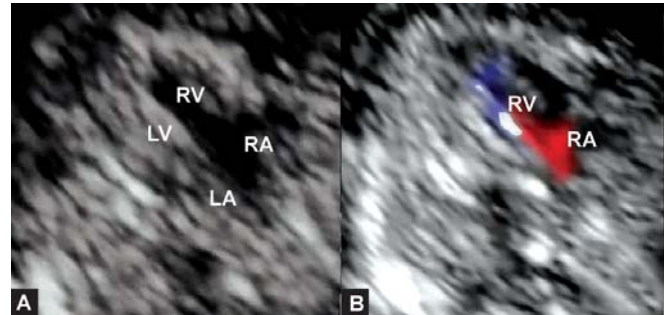
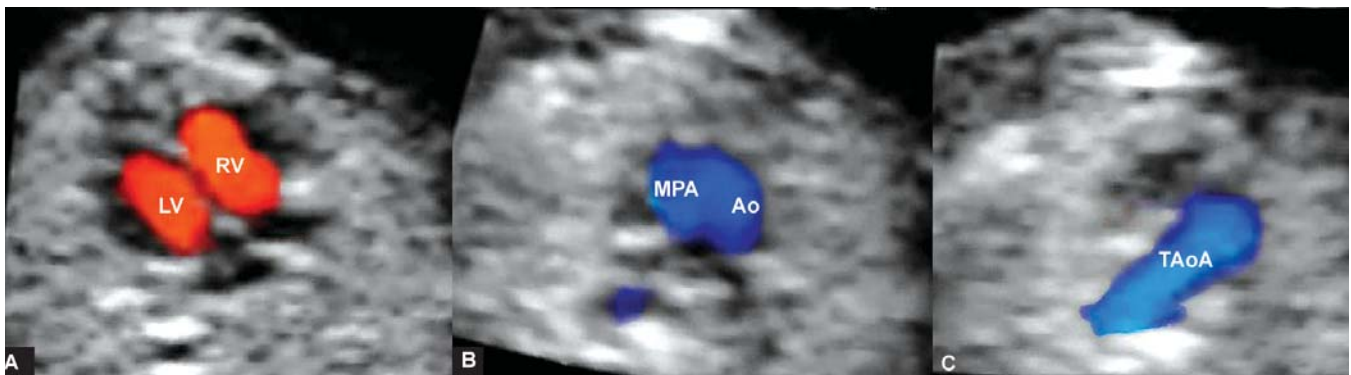


Fig. 1: Abnormal four chamber view from transabdominal approach in the first trimester fetus with CRL of 81 mm diagnosed with atrio-ventricular septal defect (AVSD) and Trisomy 21. Crux of the heart is absent



Figs 2A and B: Abnormal four chamber view in gray scale (A) and color Doppler (B) imaging demonstrating hypoplastic left heart syndrome diagnosed in the first trimester (CRL = 71 mm). Only the right sided inflow is seen in color mapping



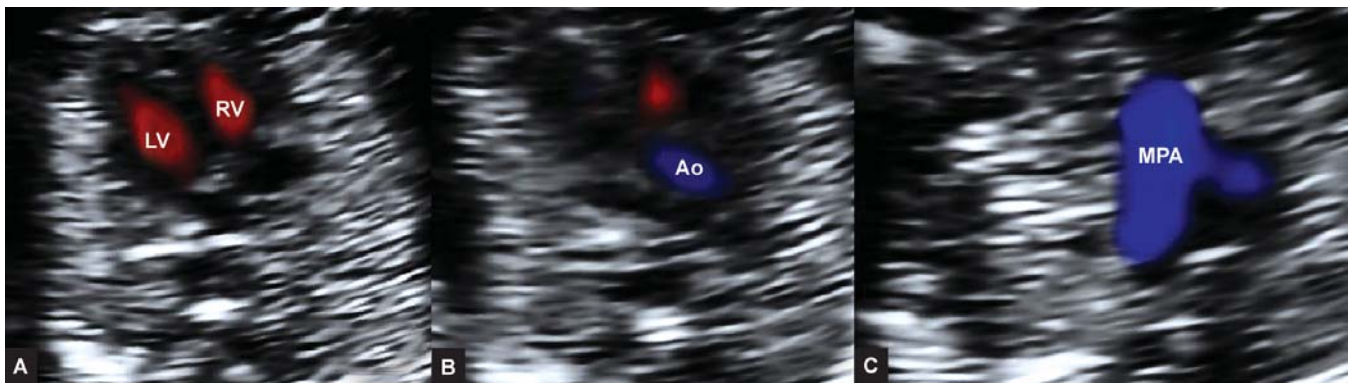
Figs 3A to C: First trimester transabdominal echocardiogram in a fetus with CRL of 72 mm diagnosed with D-transposition of great arteries demonstrates: (A) inflow to the ventricles at the level of four chamber view; (B) parallel signals of outflow tracts at the level of right outflow; (C) one arterial leg of the V-sign- trasverse aortic arch (TAoA) at the level of three vessel and trachea view (3VT)

Table 1: Details of the performed studies on effectiveness of early fetal echocardiography. Sensitivity, specificity, false positive rates, number of congenital heart defects, number of subjects in analyzed groups, equipment and population characteristics are listed

Author	Sensitivity (%)	Specificity (%)	FPR (%)	n	Group	Equipment	Population
McAuliffe et al. 2005 ²⁶	60	98	1.4	20	160	HDI 5000 TA 3-5 MHz; 4-7 MHz, opt. TV 5-8 MHz	High risk
Smrcek et al. 2006 ⁶	63	NR	NR	46	2165	HDI 5000/TA 4-7, opt. TV 4-8 MHz; Acuson 128XP: TA 4 MHz, 5 MHz TV	Mixed risk
Weiner et al. 2008 ²⁷	68.4	97	2.8	19	200	Logiq 9/Voluson 730: TA 4.5 MHz, opt. 6.5 MHz TV	High risk
Huggon et al. 2002 ²⁸	75.7	98.5	9.7	60	415	Accuson Aspen: TA 7 MHz	High risk
Becker et al. 2006 ³	84.2	NR	NR	38	3094	Accuson Sequoia: TA 8-14 MHz opt. TV	Mixed risk
Lombardi et al. 2007 ²⁰	100	100	0	3	608	Accuson Sequoia: TA linear 15 MHz, linear 6 MHz	High risk



Figs 4A to C: First trimester transvaginal echocardiogram in a fetus with CRL of 68 mm demonstrates: (A) four chamber view; (B) left ventricular outflow tract; (C) right ventricular outflow tract



Figs 5A to C: First trimester transvaginal color Doppler echocardiogram in a fetus with CRL of 68 mm demonstrates: (A) four chamber view; (B) left ventricular outflow tract; (C) right ventricular outflow tract

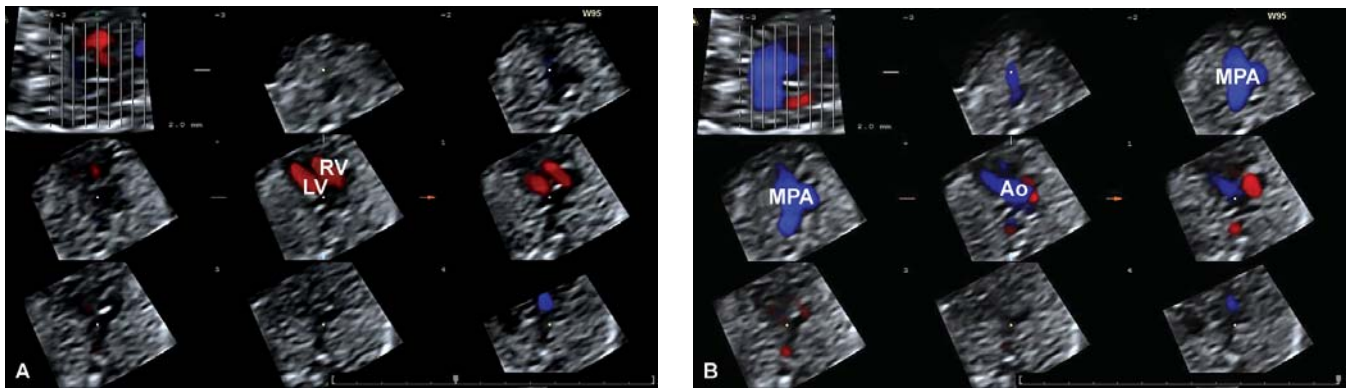
ESSENTIAL EFE COMPONENTS

There are no reasons to create examination protocol dedicated exclusively for EFE. Fetal heart between 11⁺⁰-13⁺⁶ varies only in size in comparison with second and third trimester fetal hearts. Therefore, second trimester fetal echocardiography protocol can be successfully adopted for EFE. At the beginning stomach and cardiac position, abdominal situs should be established. At the level of the 4CV: Axis, size of the heart and cardiac chambers, contractility, crux, intraventricular septum and inflow to the ventricles in color mapping should be assessed. Furthermore, both outflow tracts in gray scale and color/bidirectional power Doppler are evaluated. At the upper mediastinal level the V sign in color due to the confluence of the ductus arteriosus and the aortic isthmus at the level of three vessel and trachea view are to be examined: Examples demonstrating normal four chamber view and cross-over of great arteries in grey scale and color Doppler mapping are shown in Figures 4A to 5C. Sagittal views

provide with ductal, aortic arch and long axis caval view. Pulsed wave Doppler application is a compulsory component for assessment of the flow across the tricuspid valve, through the ductus venosus and any suspicion of aliasing. In selected cases fetal heart biometry (cardio-thoracic ratio-CTR, right ventricular diameter-RVD, left ventricular diameter-LVD, aortic diameter-AoD, main pulmonary artery diameter-MPAD) is recommended as well as pulsed wave Doppler velocimetry in great arteries.^{23,29} Medians for PSV in both great arteries are at the level of approx 30 cm/s between 11 and 13 weeks of gestation.²⁹

SPATIAL AND TEMPORAL IMAGE CORRELATION (STIC)

Spatial and temporal image correlation combines the advantages of volume imaging with the application of fetal echocardiography. In a single STIC dataset all of the basic cardiac views can be assessed along with secondary views in motion in multiple viewing planes as it is shown in Figures 6A and B.



Figs 6A and B: Tomographic ultrasound imaging display in STIC mode. Slices through the first trimester fetal heart are shown in diastole (A) and systole (B) the volume was acquired from the fetus measuring 66 mm of CRL

When a small object, such as the first trimester fetal heart, is acquired into a volume, the angle of acquisition needs to be set according to its size, and the time of capture should be as short as possible. Latest publications showed that STIC is feasible in the first trimester and broadens the application of early fetal echocardiography.^{11,30,31}

DISCUSSION

Early fetal echocardiography is feasible and reasonable. It gives parents the opportunity to exclude approximately 60% of cardiac abnormalities and to reassure them of normal heart anatomy as early as possible. Moreover early diagnosis allows for shortening of the parental decision-making process.

It is remarkable to emphasize, that EFE is highly specialistic examination and requires high expertise in early anomaly scan and fetal echocardiography. In authors opinion transvaginal approach is essential and adequate transvaginal examination is a must for clear demonstration of cardiac structures and for dispelling operator doubts.

Taking in to account EFE limitations follow-up mid-gestational echocardiography should be proposed in every single case.^{1,9}

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