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ORIGINAL ARTICLE

WILEY Congenital Heart Disease

Impact of changing indications and increased utilization of fetal echocardiography on prenatal detection of congenital heart disease

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Abstract

Background: Antenatal diagnosis of congenital heart defects (CHD) can impact outcomes in neonates with severe CHD. Obstetric screening guidelines and the indications for fetal echocardiography (FE) have evolved in an attempt to improve the early prenatal detection of CHD. Analyzing yield for specific indications will help clinicians better stratify at-risk pregnancies.

Methods: Retrospective cohort study of all FE performed between 2000 and 2010 at a single tertiary care academic medical center in New York City. A total of 9878 FE met inclusion criteria for our study. In cases of multiple gestations (MG), each fetus was counted as a separate study.

Results: The number of new diagnosis of fetal CHD by FEs increased 200%. There was a statistically significant increase in those referred for suspected CHD, increased nuchal translucency (NT), MG, and suboptimal imaging ($P < .001$). The indication of "suboptimal imaging" (SO) not only accounted for 5.23% of all referrals from 2000 to 2002, compared to 22.26% of all referrals from 2008 to 2010 ($P < .0001$), but also had the lowest yield for diagnoses of CHD ($P < .02$).

Conclusions: Over the past decade, there has been an increase in utilization of FE with a proportional increase in prenatally diagnosed CHD. For indications such as suspected CHD, NT and MG increases in referrals have led to a proportionate increase in fetal diagnosis of CHD. SO as an indication has the lowest yield of fetal diagnosis of CHD. Antenatal detection of CHD may be improved by a change in obstetric imaging protocols to ensure appropriate referrals.

KEYWORDS

congenital heart disease, fetal echocardiography, obesity

1 | INTRODUCTION

Congenital heart defects (CHD) remains the most prevalent congenital malformation, with an estimated prevalence of 6-8 per 1000 live births.[1,2] Up to a quarter of these affected newborns require some form of neonatal intervention.[3] Although tremendous strides in the diagnosis and management of CHD have been made, these lesions remain the most common cause of mortality in the developed world during the first year of life.[4,5] In addition, the severity, duration, and presence of hypoxia associated with cyanotic lesions has been previously linked to impairments of cognitive and physical development.[6]

Antenatal diagnosis may impact outcomes in neonates with CHD.[7,8] Fetal echocardiography (FE) remains the gold standard for identification of at risk pregnancies. In various low-risk as well as unselected groups, FE has excellent sensitivity at picking up major defects.[9] However, the sensitivity of a FE in properly identifying structural defects is directly correlated to operator experience and may differ by more than 30% depending on operator training.[9,10] Timely and accurate prenatal diagnosis with FE can significantly reduce, often

circumvent, delay in treatment, and, may allow for fetal intervention. Diagnosis enables early medical, socioeconomic, and psychological interventions via a multidisciplinary team of cardiologists, neonatologists, maternal-fetal medicine specialists, geneticists, nurses, and social workers.

Given the complex interplay of multiple subspecialties in the management of a disease process with implications that extend beyond immediate surgical correction and/or palliation, continued efforts have been made to identify factors which put a fetus at increased risk of developing CHD and to allow stratification of at risk pregnancies appropriately to maximize the diagnosis of fetuses with CHD and minimize unnecessary referrals. Obstetric screening guidelines and the indications for FE have evolved in an attempt to improve the early prenatal detection of CHD. Additionally, the increased prevalence of advanced parental age, multiple gestations (MG) and obesity over the past decade has affected the referral patterns for FE.

The purpose of this retrospective cohort study was to evaluate whether these changes in indications for FE led to an increased utilization of FE and/or increased fetal diagnosis of CHD by analyzing the trends in relative proportions of indications which led to a request for a FE being performed at a single tertiary care center in New York City.

2 | METHODS

We conducted a retrospective cohort study of all FE performed at the FE Laboratory at the Mount Sinai-Kravis Children's Hospital from January 2000 to December 2010.

All FE performed in that time period were included. In cases of MG, each fetus was counted as a separate study. In fetuses that had multiple examinations during the study period, only the first study was counted. When available, the primary indication, as listed by the referring physician, was noted. In cases where the referring physician listed more than one indication, a secondary indication was noted.

Indications for all FE performed during this time period were categorized. For ease of statistical analysis, these indications were grouped into ten categories shown in Table 1. Studies wherein fetuses were diagnosed with CHD were identified.

A FE was considered positive if it led to the diagnosis of structural heart disease, fetal arrhythmia, cardiac tumor, or ventricular dysfunction. Failure to meet these aforementioned diagnostic criteria led to a negative designation.

Statistical analyses were performed using SPSS (Armonk, NY). Normally distributed continuous variables were assessed using the Student's *t* test. A Mantel–Haenszel test was used to analyze the trends in relative proportions. The referral pool was then separated into four time periods and a Bonferroni correction was applied to detect trends in absolute numbers of referrals per indication and the percentage of each indication toward the total number of referrals. P values $< .05$ were considered statistically significant.

TABLE 1 List of 10 indications used to categorize all referral indications for fetal echocardiograms performed during this study period. Some indications were combined for ease of statistical analysis

Primary indication for fetal echocardiogram
• Maternal antibodies
• Maternal diabetes mellitus (Type 1 & 2, Gestational, Insulin Dependent & insulin nondependent)
• Other maternal risk factors
◦ Teratogen exposure
◦ Phenylketonuria
◦ Advanced maternal age
• Congenital heart defect suspected in fetus
• Fetal arrhythmia
• Increased nuchal translucency and/or hygroma
• Twins & multiple gestations
• Other fetal risk factors
◦ Extra-cardiac anomalies
◦ Chromosomal anomalies
• Family history of congenital heart disease
• Suboptimal cardiac imaging on obstetric ultrasound

3 | RESULTS

Over the 10-y study interval, multiple operators performed a total of 9878 FE meeting inclusion criteria. From January 2000 to December 2010, we witnessed a linear increase in the total number of patients referred for FE by more than 235%; from 587 referrals to 1398 referrals per year (Figure 1).

A total of 851 FEs were considered "positive" as they led to the diagnosis of CHD in the fetus. The number of positive FEs increased 200% over the study period from 57 positive FEs in 2000 to 107 in 2010 (Figure 1). This increase was nearly proportional to the increase in total FEs performed during the study interval.

In the initial study period, there was an increase in the percentage yield of positive FE, however, overall, there was a downward trend in annual yield over the length of our study interval; decreasing from a yield of 8.69% in 2000 to 7.65% in 2010 (Figure 2).

While referrals for most indications increased over this time period; there was a statistically significant increase in those referred for, suspected CHD, increased nuchal translucency (NT), MG, and suboptimal imaging (SO) (Figure 3) ($P < .001$). Referrals for indications such as, maternal diabetes mellitus, fetal arrhythmia, family history of congenital heart disease, fetal risk factors, maternal antibodies, and maternal risk factors remained relatively stable over the study interval.

Suspected CHD remained the indication with the highest yield, which remains consistent with previous literature regarding FE screening[11] (Figure 4).

The indication of SO had the highest impact on the increase in FE utilization compared to all other indications. Table 2 depicts the trend in absolute numbers of referrals for the indications in four periods during the study interval and the percentage of each indication toward the total number of referrals. SO accounted for 5.23% of all referrals from 2000 to 2002; however, it accounted for 22.26% of all referrals from

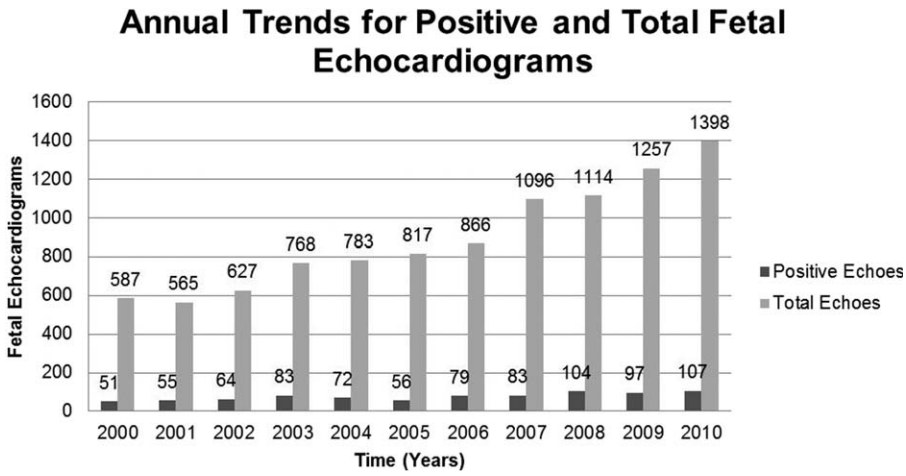


FIGURE 1 Total number of fetal echoes performed per year as well as the total of number of fetal echoes which were considered positive over a 10-y period from 2000 to 2010

2008 to 2010. ($P < .0001$) SO also had the lowest yield for diagnoses of CHD thus resulting in an overall decrease in yield of FE in the diagnosis of fetal CHD ($P < .02$) for the entire cohort.

After application of a Bonferroni correction, we detect significant trends for almost every indication, whether in a positive or negative direction, except for the indications of maternal antibodies, and other fetal and maternal risk factors (Table 2). It can be concluded that the make-up of the patients that is referred for FE today is different from that at the beginning of the study.

4 | DISCUSSION

Although previous studies have also sought to analyze indications for FE and their respective yield in the diagnosis of CHD, our study represents the largest retrospective database review of FE studies for this purpose to date.[12]

There now exists data-driven criteria prompting referral to a fetal cardiologist, guidelines for screening for structural heart defects on routine obstetric sonograms, increased awareness among practitioners, and the availability of better ultrasound technology. Yet, at the end of our study period, our institution appears to be performing more FE to diagnose proportionally fewer fetuses with CHD. Although the decline in yield is not substantial, we expected that adherence to guidelines and established criteria would have led to an increase in yield.

We hypothesize that this decline in yield may be attributable to two possible scenarios: It may be secondary to decreased referrals for high performing indications or secondary to increased referrals for low performing indications. Our data supports the latter scenario, particularly with respect to the indication of SO, which as previously noted, simultaneously contributed the largest proportion of referrals and the lowest yield.

"Suboptimal imaging," which oftentimes is secondary to the inability to image the fetal heart in an obese woman, potentially represents a

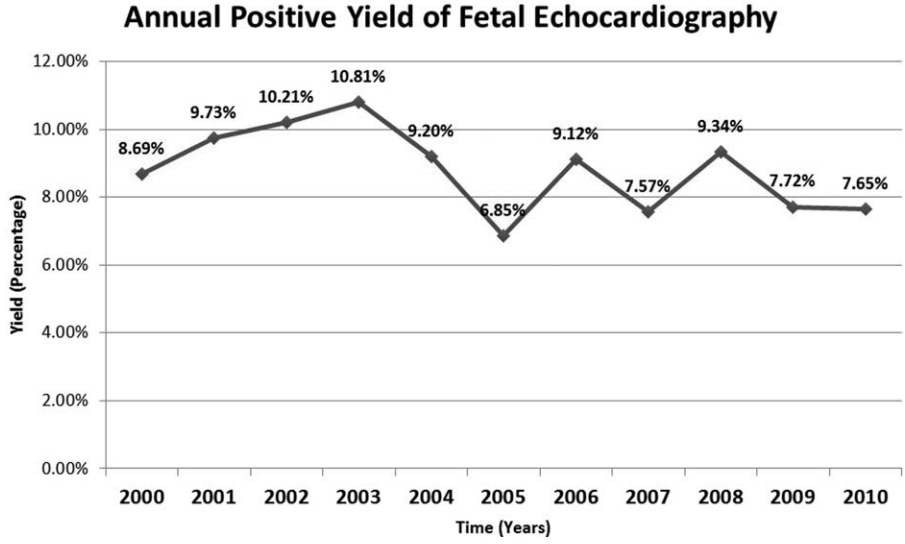
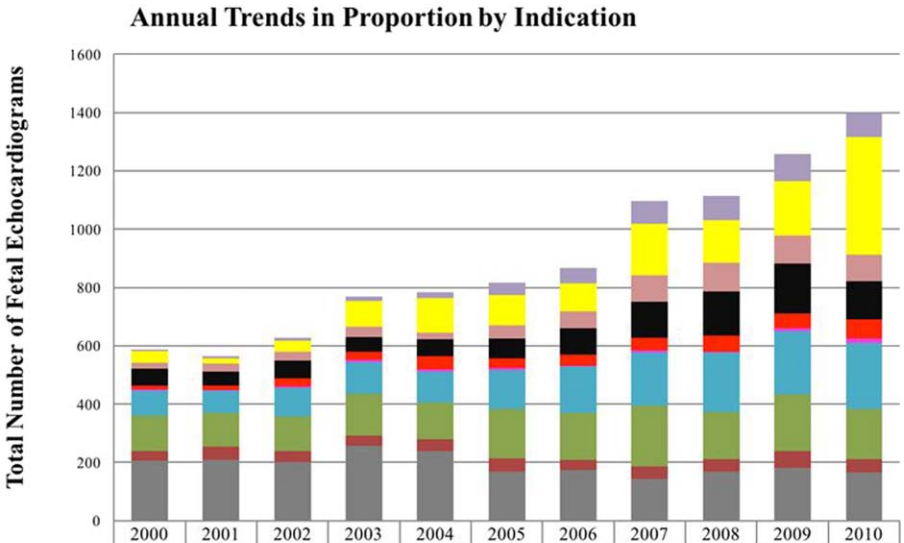


FIGURE 2 Annual overall total yield. Yield was defined as the number of fetal echocardiograms which resulted in a positive diagnosis of CHD as a percentage of all fetal echocardiograms during a given time interval. An overall decrease in yield can be seen in this study interval



	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Nuchal and Hygroma	6	8	11	15	19	44	52	78	83	93	82
Suboptimal	39	17	37	87	120	102	97	177	146	186	405
Twins/Multiples	21	29	30	37	23	47	56	90	99	96	90
Suspect CHD	58	47	61	50	58	68	91	123	152	172	131
Other Maternal Risk Factors	13	15	27	28	43	33	38	44	55	49	65
Maternal Antibodies	4	4	4	8	8	6	2	8	3	12	16
Other Fetal Risk Factors	85	76	99	108	106	134	159	180	204	216	227
Family History of CHD	121	116	118	143	127	170	162	210	160	193	172
Arrhythmia	33	44	38	35	39	44	35	42	44	60	44
Diabetes Mellitus	207	209	202	257	240	169	174	144	168	180	166

FIGURE 3 Annual trends in proportion by indication. In terms of absolute referrals, indications of maternal diabetes mellitus, fetal arrhythmia, family history of congenital heart disease, fetal risk factors, maternal antibodies, and maternal risk factors remained relatively stable across the study period. Referrals for suspected congenital heart defect in the fetus, multiple gestation, suboptimal imaging, and nuchal translucency have significantly increased

microcosm of today's practice of prenatal diagnosis of CHD in a medical landscape influenced by a variety of legal and socioeconomic factors, which extend far beyond operator skill. Furthermore, while referral patterns vary from institution to institution due to the heterogeneous ethnic, social, and economic demographics that comprise their patient population, the national impact, prevalence, and increase in obesity throughout all facets of American society make this an indication that can be easily extrapolated to the greater U.S. population as a whole.[13,14]

Currently, there is no formal consensus on the impact of maternal obesity on the developing fetal heart as the majority of the literature assessing the causal relationship of CHD and weight status have

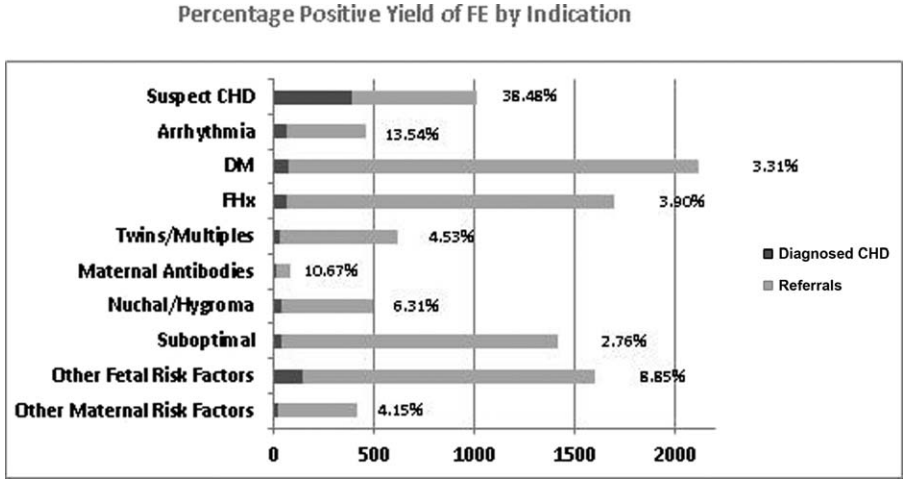


FIGURE 4 Percentage positive yield of fetal echocardiography by indication. Those referred for suspected CHD had the highest yield while those referred for suboptimal imaging had the lowest

TABLE 2 Trend in absolute numbers of referrals for the indications in four periods during the study interval and the percentage of each indication toward the total number of referrals

	Period						
	2000-2002	2003-2005	2006-2008	2009-2010	Total	*P* for trend (vs others)	*P* for trend (Bonferroni)
Suspect CHD							
N	166	176	366	303	1011	<.0001	<.001
%	9.33	7.43	11.9	11.41			
Fetal arrhythmia							
N		118	121	104	458	<.0001	<.001
%	6.46	4.98	3.93	3.92			
Diabetes mellitus							
N	618	666	486	346	2116	<.0001	<.001
%	34.74	28.13	15.8	13.03			
Family history							
N	355	440	532	365	1692	<.0001	<.001
%	19.96	18.58	17.3	13.75			
Twin-multiples							
N	80	107	245	186	618	<.0001	<.001
%	4.5	4.52	7.96	7.01			
Maternal antibodies							
N	12	22	13	28	75	.45	1
%	0.67	0.93	0.42	1.05			
Nuchal and hygroma							
N	25	78	213	176	491	<.0001	<.001
%	1.41	3.29	6.92	6.59			
Suboptimal imaging							
N	93	309	420	591	1413	<.0001	<.001
%	5.23	13.05	13.65	22.26			
Other fetal risk factors							
N	260	348	543	443	1594	.0080.08	
%	14.61	14.7	17.65	16.69			
Other maternal risk factors							
N	55	104	137	114	410	.09	.88
%	3.09	4.39	4.45	4.29			

Applying the Bonferroni correction, we detect significant trends for every indication, except for the indications of maternal antibodies, fetal risk factors, and maternal risk factors.

revealed either weak associations or no association at all.[15] In instances in which stronger associations have been shown, there remains a lack of evidence to definitively declare causality to the extent of warranting further cardiac screening beyond initial obstetric sonography. Often times, there are other maternal risk factors that tend to co-present in overweight mothers (eg, diabetes).[15] These risk factors, however, have been shown to directly impact fetal heart development and, under the current guidelines would warrant referral to a pediatric subspecialist for a FE.[12]

If maternal body habitus is not an official indication for referral, why, over the course of our study, have we seen a consistent and marked increase in referrals for this indication? The revised guidelines for cardiac screening call for obtaining more images than in the past, not just a four-chamber view of the heart but also a view of crossing great vessels. These guidelines cite the work of Viñals et al, which demonstrated the benefit of three Vessel-Trachea View and recommended its routine use in screening for CHD.[16] However, obtaining this view might not be achievable because of skill limitations in the technician obtaining the images, difficulty in visualizing the heart in some fetuses, and most importantly because of the change in the body habitus of the pregnant population today.

If referrers are unable to "sign-off" on their initial screening, they may find it necessary to refer the patient for secondary screening despite their low-risk status for carrying a fetus with CHD. It is worth noting that the publication of Viñals et al's study in 2003 coincides

with the increased referral rate in our patient population for "suboptimal imaging."

It can be argued that a push for increased screening is warranted given the benefit of antenatal diagnosis in the management of neonates with CHD. The failure of increased screening leading to an increase in the overall detection rate in our study population may indicate that casting a "wide net" may lead to a larger catch but not to a more "appropriate" catch. This latter point is increasingly relevant in today's health care environment, which continues to remain focused on reducing unnecessary health care utilization in an effort to alleviate its increasing costs.

Recent literature assessing the economic impact of diagnosing fetal heart defects using various modalities currently available revealed that FE, performed by an experienced pediatric cardiologist or maternal-fetal specialist is the most expensive test to diagnose CHD.[10] Cost-benefit analysis would then dictate that this test be used only in a subset of fetuses that are determined to be at increased risk of having CHD. It is important to differentiate between absolute cost and cost-effectiveness of FE, as cost-effectiveness is dictated by how much the population at large is willing to spend to reduce risk.

This change in referral indications also highlights an important gap between development of health care standards and education infrastructure to meet the requirements of the published standards. In the end, obstetric ultrasound technicians can be trained to better assess the fetal heart, but in the case of the large pregnant patient, more research is required to stratify those at a higher risk of having a fetus with CHD. This might mean employing markers such as NT in tandem with other modalities given the correlation between increasing incidence of major CHD with increasing NT measurements.[17] Another approach would be to adopt a different modality of screening patients whose body habitus presents a challenge to the imaging of the fetal heart. First-trimester echocardiography, with transvaginal approaches, may result in earlier visualization of defects that may otherwise be inaccessible and represents a promising avenue of research.[18] Other advanced ultrasound techniques such as harmonics imaging may also prove useful.[19,20]

An alternative way of analyzing this issue would be that the guidelines suggested by the writing group of the American Heart Association recommends obtaining a FE for all indications which confer a risk of 3% or more for congenital heart disease.[21] In that case, it would be expected that the positive yield of FE would drift lower if studies are obtained for these indications.

Finally, the burden of increased referrals should not be solely placed on the primary referrer. Changes in imaging guidelines and the inherent complex nature of fetal cardiac imaging as indicated by varying detection rates given one's level of training, creates an environment in which we have prescribed undue expectations upon our referrer pool. Isolating and detecting at risk pregnancies requires the interplay of a variety of pediatric and obstetric subspecialists. Thus, increasing awareness of congenital heart disease amongst practitioners must extend beyond education focusing on who needs a test and why; it must also involve increased and adequate secondary training. This can be accomplished by integrating more imaging training in the referrer population, or by assuring that the expectations and goals for pre-referral imaging are reasonable in their achievability.

5 | CONCLUSION

Over the last decade, there has been an increase in utilization of FE with a proportional increase in prenatally diagnosed CHD. For indications such as suspected CHD, NT and MG increases in referrals have led to a proportionate increase in fetal diagnosis of CHD. Although referral for SO has contributed the most to utilization of FE resources, it has the lowest yield of fetal diagnosis of CHD at our institution. Strategies that balance obstetrical imaging training modalities to decrease referrals for low yield indications in this patient population, coupled with increased utilization of FE for indications with a high yield should continue to improve the antenatal detection of CHD.

CONFLICT OF INTEREST

The authors have no potential conflicts of interest to disclose.

FINANCIAL DISCLOSURE

The authors have no financial relationships relevant to this article to disclose.

AUTHOR CONTRIBUTORS

Mr. Komisar carried out the initial analyses, drafted the initial manuscript, and approved the final manuscript as submitted.

Dr. Srivastava conceptualized and designed the study, reviewed and revised the manuscript, and approved the final manuscript as submitted.

Dr. Geiger and Ms. Ko supervised data collection, reviewed the manuscript, and approved the final manuscript as submitted.

Dr. Doucette carried out statistical analyses, reviewed the manuscript, and approved the final manuscript as submitted.

Mr. Shenoy carried out data collection and initial analyses, reviewed the manuscript, and approved the final manuscript as submitted.

Dr. Shenoy conceptualized and designed the study, supervised data collection, critically reviewed and revised the manuscript, and approved the final manuscript as submitted.

REFERENCES

[1] Hoffman JIE, Christianson R. Congenital heart disease in a cohort of 19,502 births with long- term follow-up. *Am J Cardiol.* 1978;42(4):641–647.

[2] Allan L, Benacerraf B, Copel JA, et al. Isolated major congenital heart disease. *Ultrasound Obstet Gynecol.* 2001;17(5):370–379.

[3] Oster ME, Lee KA, Honein MA, Riehle-Colarusso T, Shin M, Correa A. Temporal trends in survival among infants with critical congenital heart defects. *Pediatrics.* 2013;131(5):e1502–e1508.

[4] Yang Q, Chen H, Correa A, Devine O, Mathews TJ, Honein MA. Racial differences in infant mortality attributable to birth defects in

the United States, 1989-2002. *Birth Defects Res Part A Clin Mol Teratol.* 2006;76(10):706–713.

[5] Gilboa SM, Salemi JL, Nembhard WN, Fixler DE, Correa A. Mortality resulting from congenital heart disease among children and adults in the United States, 1999 to 2006. *Circulation.* 2010;122(22):2254–2263.

[6] Newburger JW, Silbert AR, Buckley LP, Fyler DC. Cognitive function and age at repair of transposition of the great arteries in children. *N Engl J Med.* 1984;310:1495–1499.

[7] Bonnet D, Coltri A, Butera G, et al. Detection of transposition of the great arteries in fetuses reduces neonatal morbidity and mortality. *Circulation.* 1999;99(7):916–918.

[8] Franklin O. Prenatal diagnosis of coarctation of the aorta improves survival and reduces morbidity. *Heart.* 2002;87(1):67–69.

[9] Randall P, Brealey S, Hahn S, Khan KS, Parsons JM. Accuracy of fetal echocardiography in the routine detection of congenital heart disease among unselected and low risk populations: a systematic review. *BJOG.* 2005;112(1):24–30.

[10] Pinto NM, Nelson R, Puchalski M, Metz TD, Smith KJ. Cost-effectiveness of prenatal screening strategies for congenital heart disease. *Ultrasound Obstet Gynecol.* 2014;44(1):50–57.

[11] Sharony R, Fejgin MD, Biron-Shental T, Hershko-Klement A, Amiel A, Levi A. Who should be offered fetal echocardiography? One center's experience with 3965 cases. *Isr Med Assoc J.* 2009;11(9):542–545.

[12] American Institute of Ultrasound in Medicine. AIUM practice guideline for the performance of fetal echocardiography. *J Ultrasound Med.* 2013;32(6):1067–1082.

[13] Moore LL, Singer MR, Bradlee ML, Rothman KJ, Milunsky A. A prospective study of the risk of congenital defects associated with maternal obesity and diabetes mellitus. *Epidemiology.* 2000;11(6):689–694.

[14] Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of Childhood and Adult Obesity in the United States, 2011-2012. *J Am Med Assoc.* 2014;311(8):806.

[15] Cai G, Sun X, Zhang L, Hong Q. Association between maternal body mass index and congenital heart defects in offspring: a systematic review. *Am J Obstet Gynecol.* 2014;211(2):91–117.

[16] Viñals F, Heredia F, Giuliano A. The role of the three vessels and trachea view (3VT) in the diagnosis of congenital heart defects. *Ultrasound Obstet Gynecol.* 2003;22(4):358–367.

[17] Clur SA, Mathijssen IB, Pajkrt E, et al. Structural heart defects associated with an increased nuchal translucency: 9 years experience in a referral centre. *Prenat Diagn.* 2008;28(4):347–354.

[18] Mirza F, Bauer S, Williams I, Simpson L. Early fetal echocardiography: ready for prime time? *Am J Perinatol.* 2012;29(04):313–318.

[19] Paladini D, Vassallo M, Tartaglione A, Lapadula C, Martinelli P. The role of tissue harmonic imaging in fetal echocardiography. *Ultrasound Obstet Gynecol.* 2004;23(2):159–164.

[20] Kovalchin JP, Lewin MB, Bezold LI, Altman CA, Ayres NA. Harmonic imaging in fetal echocardiography. *J Am Soc Echocardiogr.* 2001;14(10):1025–1029.

[21] Donofrio MT, Moon-Grady AJ, Hornberger LK, et al. Diagnosis and treatment of fetal cardiac disease – a scientific statement from the american heart association. *Circulation.* 2014;129:2183–2242.

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