The developing role of fetal magnetic resonance imaging in the diagnosis of congenital cardiac anomalies: A systematic review

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ABSTRACT

Advances in the fetal magnetic resonance imaging (MRI) over the last few years have resulted in the exploring the use of fetal MRI to detect congenital cardiac anomalies. Early detection of congenital cardiac anomalies can help more appropriately manage the infant's delivery and neonatal management. MRI offers anatomical and functional studies and is a safe adjunct that can help more fully understand a fetus' cardiac anatomy. It is important for the obstetricians and pediatric cardiologists to be aware of the recent advancements in fetal MRI and it`s potential utility in diagnosing congenital cardiac anomalies.

Keywords: Cardiac anomalies, congenital heart disease, fetal diagnosis, magnetic resonance imaging

INTRODUCTION

Fetal cardiac examination is an important part of obstetrical follow-up during pregnancy and impacts future care of the infant. Fetal diagnosis allows for specially tailored preparations to be made for the delivery and early care of an infant with congenital cardiac anomalies (CCA). CCA affects nearly 9 per 1,000 live births and represents the largest subclass of congenital anomalies.[1] Early detection of these lesions can ensure that the delivery occurs in a unit where the infant can receive specialized care where likelihood of morbidity and mortality may be decreased.

Echocardiography has been the primary method of fetal anatomic surveys, including cardiac surveys. With advancements in magnetic resonance imaging (MRI) technology, fetal MRI's utility in detecting CCA is increasing.

DOCUMENTED CLINICAL EXPERIENCE

Fetal MRI has been used to diagnose various forms of CCA such as cardiac rhabdomyoma,[2] truncus arteriosus,[3] isolated levocardia,[4] and others.[5-9] A retrospective study recently defined fetal MRI findings to detect twin reversed arterial perfusion sequence in monochorionic pregnancies.[10]

Manganaro, *et al.*, first reported their experience with cardiac MRI in a study of 31 fetuses, all with no cardiothoracic abnormalities noted on echocardiography. The study set out to determine what could be reliably obtained from cardiac survey with fetal MRI. Heart size was compared to the thorax, the cardiac apex located, ventricular septal thickness and angulation determined, structure and size of the cardiac chambers was determined, and cardiac function was evaluated. Cardiac MRI also allowed for delineation of the aorta, determining size and position of the pulmonary artery, aorta, and superior vena cava. The ductus arteriosus was also detected although the pulmonary veins were not detected.[7]

Ventricular shape and relative position and ventricular kinetics were also assessed by cardiac MRI. A retrospective analysis of ten fetal cardiac MRI studies, by Gorincour, *et al.*, added the assessment of ventricular looping as being possible in all fetuses as well.[9] A 20-fetus study by Saleem, *et al.*, also concluded that cardiac MRI can be used to determine the cardiac parameters outlined by Mangano and Gorincour.[10] These findings demonstrate that fetal MRI can be used as an additional tool in CCA diagnosis.

Manganaro, *et al.*, then reported a study of cardiac MRI on 32 fetuses, all of which demonstrated CCA on

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echocardiogram. CCA assessments were made on the basis of direct and indirect signs, with 17 fetuses having CCA diagnosed by direct MRI signs, five by indirect signs, and nine by both direct and indirect. MRI ruled out a suspected diagnosis of hypoplastic left heart syndrome made in one fetus by echocardiograph. A variety of lesions was diagnosed by MRI use. This study, thus, established the feasibility of cardiac MRI in diagnosing CCA in fetuses.[8]

TECHNIQUES

Unique circumstances surrounding imaging the fetus have led to the investigation of various MRI techniques for use in this particular application. Brisk fetal heart rate and fetal movement require appropriate techniques that allow for rapid sequence MRI imaging. Two main MRI techniques are currently being utilized to accomplish this: Half acquisition single-shot fast spin echo (HASTE) and steady state free precession imaging (TrueFISP).[11,12]

The HASTE sequence uses an excitation pulse followed by subsequent refocusing pulses. Images are then sequentially restructured with short imaging times which minimizes artifact due to fetal motion. Short scan times with the HASTE sequence are possible due to recent advancements in gradient efficiency and radio frequency (RF) systems. All this translates into image acquisition at a rate of less than two seconds per slice.[13] Previously mentioned studies by Manganaro, *et al.*, Gorincour, *et al.*, and other documented case reports have utilized the HASTE technique for CCA diagnosis via fetal MRI.[2,3,7,8]

In TrueFISP gradient echo based imaging technique in which transverse magnetization is rephased after multiple, rapid excitations. Here, short echo times allow for minimization of fetal movement artifact using TrueFISP.[14,15] The study by Saleem, *et al.*, utilized this technique.[10]

Motion artifact is not the only obstacle when using cardiac MRI to image the fetus as a gating signal is usually required for such imaging as well. Cardiac MRI may be gated to an electrocardiogram or pulse monitor, neither of which is a practical method for fetal studies. There are four gating alternatives that have been described that can help overcome this.

One such alternative is real-time imaging with rapid acquisition so that no gating is required. However, the loss of temporal and spatial resolution is an issue, particularly in fetal cardiac imaging due to small fetal structures and rapid heart rates making the resulting images of questionable clinical value. Real time imaging is used to produce cine MRI which can allow for dynamic assessment of function.[16]

MRI images can also be acquired with no gating at all with use of nontriggered acquisition. Images are acquired with no concern for the cardiac phase they represent; although, the entire series of images is believed to be ample enough to represent all cardiac phases equally. There is a loss of any dynamic analysis with nontriggered acquisition and studies on the great vessels are of limited yield due to dynamic changes throughout the cardiac cycle.

Self-gating is a technique in which retrospective analysis of acquired MRI data allows for a gating signal to be extracted from the data itself. With no need for monitoring equipment, self-gated MRI is a feasible method to use for fetal cardiac studies. While there have been no documented reports of self-gated MRI being used for fetal cardiac studies in humans, Holmes, *et al.*, applied the method to chick embryos in ovo and Nieman, *et al.*, applied the method to fetal mice with good quality images.[17,18] More recently, Yamamura, *et al.*, studied self-gating on fetal sheep compared to real cardiac gating. This study found that self-gating allows for anatomical and functional evaluation with images being only slightly inferior to those acquired using real cardiac gating.[19]

Jansz, *et al.*, recently reported metric optimized gating, a new gating strategy. Misgating artifact is detected through evaluation of image metrics while images are retrospectively analyzed. This technique does require that each segment is imaged throughout the entire cardiac cycle for proper reconstruction of images. This study simulated MRI studies of fetal vessels by imaging the carotid arteries of volunteers since these vessels have a similar size to fetal great vessels. One fetus was also imaged using this technique. Both of these analyses validated this gating method.[20]

ADVANTAGES AND LIMITATIONS

When compared to echocardiography, MRI does offer some advantages when it comes to diagnosing CCA. MRI offers better estimates of chamber volume than standard echocardiography. Volume measurements made using two-dimensional echocardiography are often inaccurate due to the estimates being made with assumption of chamber shape. Particularly in patients with CCA, this could lead to gross over- or underestimation of chamber volumes. An *ex vivo* comparison of cardiac MRI and three dimensional echocardiography demonstrated greater image quality and structural detail in MRI-obtained studies.[21] This finding, however, may not necessarily extrapolate for fetal MRI at this time due to the limitations imposed by current gating techniques. Unlike echocardiography, MRI is also not limited by acoustic window. Additionally, factors such as oligohydramnios and maternal obesity don't affect fetal MRI studies.[22,23] Operator dependence of actual image acquisition is another issue with fetal echocardiography but not for fetal MRI.[24] A recent study by Yamamura, *et al.*, also demonstrated MRI's ability to allow for complete evaluation of fetal great vessels, a task often not accomplished with echocardiography.[25]

Fetal MRI does have some limitations when compared to echocardiography. Fetal movements can affect imaging although maternal sedation and recent advancements in image acquisition sequences can help alleviate some of these effects.[12,26] When compared to MRI, echocardiography also allows for simpler flow evaluation via use of Doppler and color. However, through-plane velocity does allow for flow to be estimated using MRI.[20] There is paucity of fetal MRI studies during first trimester.[27]

SAFETY

Animal studies focusing on safety of fetal MRI have had mixed results. Studies have found that mid-gestation exposure to MRI had no gross effects on mice other than a reduction in crown-rump length,[28] no effect on mortality or hatching rate of chickens,[29] no effects on cell proliferation and migration effects in chickens,[30] and no effect on axonal growth in chickens.[31] One study did note increased abnormalities and mortality rates in six day embryos after exposure to 1.5T MRI.[32] Fetal MRI studies in humans have found the following: No increase in disease during three year follow-up in children imaged in utero,[33] no impact on intrauterine fetal growth,[34] and no change in cardiotocographic measurements.[35-37]

Fetal safety of MRI relate to three major parts of the MRI: Static magnetic field, RF, and electromagnetic field (EMF). Static magnetic fields and their effects on embryogenesis have been studied with some studies finding that fields even up to 8 T did not have any negative impact on cleavage, division, differentiation, or growth of human culture cells.[38,39] Chick embryo membranes were found to be unaffected by static magnetic fields up to 5 mT[40] while a study by Mevissen, *et al.*, did document increased fetal loss when pregnant rats were exposed to 30 mT static fields.[41] Other studies have noted decreased survival fraction for mouse embryos in the two-cell stage after being exposed to a 1.5 T static field for 30 minutes,[42] delay and reduction of hatching Heliothis veriscens eggs,[43] irreversible damage in the cerebellar cortex of chicks exposed to 20 mT magnetics fields as embryos.[44] A human study focusing on pregnant MRI workers found no significant differences among pregnancy parameters in women who were exposed to MRI magnetic fields.[45] Duration of exposure is noted to be associated with more of the adverse effects noted in other animal models.

Along with the static magnetic fields employed by MRI, there are also RF fields which can cause thermal heating. Fluctuations in fetal temperature can adversely affect the fetus, particularly during times of peak organogenesis. Studies have noted increased risk of neural tube defects and craniofacial defects in babies exposed to a rise of 2°C over 24 hours. Intrauterine temperature was monitored in pregnant pigs undergoing imaging with 1.5 T MRI with no significant temperature increase observed.[46] Kawabata, *et al.*, did the same in a pregnant rabbit with similar results. While the studies noted are limited in the number of animals studied, it doesn't appear that RF induces a temperature increase harmful to the fetus in humans with standard use.

Electromagnetic gradient fields (EMF) raise questions about biological effects as well as acoustic noise. Rodegerdts *et al.*, studied the effect of EMF on fetal human fibroblasts and found no significant differences between those exposed to MRI with static field turned off and those not exposed to MRI.[47] Guisasola *et al.*, also studied EMF effect on *in-vitro* cells and found no significant effects.[48] In addition to temperature increase, EMF also has implications due to acoustic noise generated by rapid switching of currents in the coils. The result is loud knocks that can range from 80 dB to 120 dB among MRI machines.[49] Exposure of a fetus to loud sounds can result in diminished hearing during childhood. Baker *et al.*, performed a 3 year follow-up test of children imaged with fetal MRI and found that two out of 18 children failed a distraction test at the age of 8 months.[33]

Bearing all in mind, it appears that MRI used appropriately within standard parameters on 1.5 T and 3 T machines should be safe for fetuses.

CONCLUSIONS

Recent advances in imaging technology and gating have made fetal cardiac MRI feasible. MRI is a safe adjunct that can help more properly delineate both normal and abnormal cardiac anatomy. MRI may be utilized as an adjunct to fetal echocardiography when required. Further advances in technology will expand the role of fetal MRI in the diagnosis of CCA and possibly provide insights into cardiac embryogenesis in the future.

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