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Who should attend?

This interactive course is designed for Maternal Fetal Medicine (MFMs), OB-GYNs, Radiologists, Sonographers, Geneticists, Researchers, Trainees/Residents and other maternity care providers. The program will appeal to a wide global audience, with a focus on North American educational needs.

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ISUOG consensus statement on current understanding of the association of neurodevelopmental delay and congenital heart disease: impact on prenatal counseling

An association between congenital heart disease (CHD) and neurodevelopmental delay (NDD) has long been recognized, but remains poorly understood. It is almost certainly multifactorial^{1–8}. A number of abnormal magnetic resonance imaging (MRI), magnetic resonance spectroscopy (MRS) or sonographic findings, specifically abnormal or delayed sulcation, reduced brain biometry and volumes and abnormal brain biochemistry, have been described in fetuses and neonates with some forms of CHD^{9–17}. This suggests that genetic factors³ and the prenatal environment play an important role in the determination of postnatal neurodevelopmental function, in contrast to traditional concepts attributing adverse neurodevelopmental outcomes to postnatal events such as perinatal hypoxia and perisurgical damage. Furthermore, some large cohort trials have demonstrated an increased risk of NDD mainly – but not only – in children and young adults with univentricular circulation and, to a lesser extent, in those with transposition of the great arteries (TGA)^{14,18–21}. The increasing supportive evidence in this field has led to the publication of an official scientific statement by the American Heart Association²², in which the conclusions are that: ‘Children with CHD are at increased risk of developmental disorder or disabilities or developmental delay’ and, therefore, ‘...surveillance, screening evaluation and re-evaluation during childhood’ are recommended to diagnose and, if possible, treat the various aspects of these disabilities.

Experience in the interpretation of any prenatal imaging modality is paramount in assessing its ability to detect real disease and, hence, its true clinical importance. This can be gained only in the setting of well-designed studies. Furthermore, the full extent of clinically important NDD cannot be determined during the first years of a child’s life; thus, these studies also require adequate follow-up. The deficiencies in current published studies have raised genuine and widespread concerns that a discussion of possible adverse neurodevelopmental outcomes linked to CHD may lead couples to opt for termination of pregnancy in those cases of isolated CHD that are usually associated with low mortality and low long-term morbidity, such as TGA. However,

the available evidence would suggest that it is neither possible nor ethical to ignore this risk during prenatal counseling^{14,17,23}.

A recent survey, conducted by an ISUOG (International Society of Ultrasound in Obstetrics and Gynecology) Task Force to gauge the attitudes and perceptions of health professionals from leading referral units for CHD worldwide found significant differences in the way in which prenatal counseling is conducted, particularly between North American and European centers²⁴.

ISUOG has compiled the following Consensus Statement, which will be updated on a regular basis to take into account new studies in this field.

- Considering the emerging literature^{1–3}, we believe that, for the fetus with CHD, array comparative genomic hybridization (CGH) is much more appropriate than conventional karyotyping for ruling out or confirming genetic conditions that are potentially responsible for NDD in fetuses with CHD.
- Fetuses/neonates with hypoplastic left heart (HLH) and other lesions resulting in a postnatal univentricular circulation show an increased risk (> 40% in some studies^{14,18–21}) of both brain morphometric abnormalities – evident on prenatal MRI and ultrasound – and NDD, independent of surgery. During prenatal counseling for these types of cardiac lesions, we recommend mentioning that there is an increased risk of NDD. A separate statement (see below) will address the issue of how to describe the risk.
- For all other CHDs, including TGA, it is felt that current evidence should be supported by further studies of children with prenatal diagnosis and optimal perinatal management before providing the same type of counseling as for those with a univentricular circulation.
- Very preliminary data show that brain morphometric abnormalities associated with NDD in the neonate can be diagnosed in the fetus¹⁵. However, further evidence from imaging and metabolic studies, including ultrasound and MRI or MRS, are needed prior to including detailed brain imaging in the routine prenatal surveillance protocol of fetuses with CHD. Currently,

prenatal brain imaging is recommended only to detect associated malformations or as part of investigational clinical trials.

- A balanced approach to the discussion of an association between NDD and CHD is essential in order to be relevant to the many cultural, religious and legal differences in different countries. Our society suggests that the following statement may be helpful during counseling: ‘...the majority of fetuses/neonates with isolated CHD do well. However, there is evidence that some have a degree of NDD, which cannot be predicted antenatally. The severity of this impairment varies from individual to individual, and the likely incidence varies with the type of CHD, being highest (up to 40–45% in some studies) in lesions with univentricular heart hemodynamics such as HLH. We advise genetic investigations, including array-CGH to rule out associated and syndromic forms of CHD.’
- The recommendation that fetuses with a prenatal diagnosis of major CHD should be delivered in a tertiary referral center, in which multidisciplinary neonatal management is available, is reinforced on the basis of the data discussed above.
- The recommendation regarding if and when to perform postnatal ultrasound, MRI/MRS and neurodevelopmental assessment is beyond the scope of this consensus statement. We recommend that national guidelines are followed to ensure appropriate evaluation of children and adolescents with CHD.

Writing group

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