Taiwanese Journal of Obstetrics & Gynecology 54 (2015) 284–289

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Original Article

Establishment of a database of fetal congenital heart malformations and preliminary investigation of its clinical application

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ARTICLE INFO

Article history:
Accepted 27 January 2015

Keywords:
anatomic section
congenital heart disease
database
fetal

ABSTRACT

Objective: The aim of this study was to create a database of anatomical ultrathin cross-sectional images of fetal hearts with different congenital heart diseases (CHDs) and preliminarily to investigate its clinical application.

Materials and methods: Forty Chinese fetal heart samples from induced labor due to different CHDs were cut transversely at 60-μm thickness. All thoracic organs were removed from the thoracic cavity after formalin fixation, embedded in optimum cutting temperature compound, and then frozen at −25°C for 2 hours. Subsequently, macro shots of the frozen serial sections were obtained using a digital camera in order to build a database of anatomical ultrathin cross-sectional images.

Results: Images in the database clearly displayed the fetal heart structures. After importing the images into three-dimensional software, the following functions could be realized: (1) based on the original database of transverse sections, databases of sagittal and coronal sections could be constructed; and (2) the original and constructed databases could be displayed continuously and dynamically, and rotated in arbitrary angles. They could also be displayed synchronically. The aforementioned functions of the database allowed for the retrieval of images and three-dimensional anatomy characteristics of the different fetal CHDs, and virtualization of fetal echocardiography findings.

Conclusion: A database of 40 different cross-sectional fetal CHDs was established. An extensive database library of fetal CHDs, from which sonographers and students can study the anatomical features of fetal CHDs and virtualize fetal echocardiography findings via either centralized training or distance education, can be established in the future by accumulating further cases.

Introduction

Fetal congenital heart disease (CHD) is the leading cause of infant death [1–3]. For pregnant women, an antenatal diagnosis of seriously complicated CHD can not only reduce the birth rate but also improve the success rate of surgery after birth, with the help of prenatal counseling [4–6]. Fetal echocardiography (FECG) is the main method of prenatal diagnosis of CHD. However, due to the effects of an unstable fetal position, rapid heart rate, subtle heart structures, and special fetal circulations (intrauterine blood flow properties in the foramen ovale and ductus arteriosus), as well as other limitations, FECG is more difficult to perform than adult echocardiography. Consequently, the technology is still not popular. The rate of antenatal diagnosis varies between countries, including between developed countries [7–10]. Further, the lack of understanding about the anatomical structures also makes it difficult to interpret FECG findings. A database of fetal heart anatomies can be used to better understand the anatomical features of the different CHDs and to virtualize FECG using three-dimensional (3-D) software. The sectional anatomical and 3-D models of the adult heart [11–16] from the first Chinese Digital Human [17] and Visible Human Project [18] have been applied in scientific research, school education, and clinical research. However, no research regarding the applicability of a fetal heart database has been reported. In 2010, we reported the first-ever database established for the normal fetal heart anatomy [19]. Since then, we have established a database with fetal heart images of 40 cases with CHD. This paper reports the characteristics of these cases and presents the results of

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http://dx.doi.org/10.1016/j.tjog.2015.01.002

our preliminary analysis of the clinical application value of our database.

Materials and methods

Source of the specimens

Forty fetal samples from induced labor due to CHD with or without malformations in other systems were included in this study. All samples were Chinese fetuses. This study was conducted in accordance with the Declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Peking University People's Hospital, Beijing, China. Written informed consent was obtained from all participants' guardians.

Pretreatment of the samples

The skin and subcutaneous tissue of the pleura were cut along the left sternal border of the fetal sample, and the tissue samples were fixed with 4% formaldehyde for 4–8 weeks. Subsequently, the thymus, lungs, heart, trachea, esophagus, descending aorta, and part of the inferior vena cava were separated and removed as a whole from the thoracic cavity. Afterward, we continued fixing the thoracic viscera for 2–4 weeks. Next, the heart sample was removed, along with a 0.5-cm-thick border of lung tissue on the sides to maintain the maximum size that would fit into the freezing microtome.

Installation of the logo bar and establishment of the original database of transverse sections

A square organic glass box (size: 4 cm × 4.5 cm × 4.5 cm or 5 cm × 5.5 cm × 5.5 cm), with hole grooves of 0.3 cm in diameter in the four corners of the box cover and base was used. According to the different gestational ages, we placed the pretreated heart sample into the box vertically to submerge the heart sample in optimum cutting temperature compound and covered the box. Next, we inserted 2–4 pencil leads (0.3 cm in diameter) vertically from the hole in the cover to the base hole groove. After being frozen for 4 hours at −25°C, we took out the content of the box as a whole and fixed it using a freezing microtome (CM1900; Leica, Wetzlar, Germany). From the base to the top, the heart samples were cut transversely to 60-μm thickness, and every section was macroshot with a digital camera (EOS 5D Mark II; camera lens, EF180mm f/3.5L Macro; Canon, Tokyo, Japan); the anatomical ultrathin cross-sectional images of the different fetal CHDs obtained were used to build the original database. Each

Table 1
Forty case cross-section databases of fetal heart with congenital heart disease (CHD).

CHD types	Gestational age (wk)	Case number	Diagnostic basis
ECD	25	2	Biopsy
ECD	12	1	Biopsy
ECD + DOVT + PAS + APVC	28	1	Biopsy
ECD + APVC	22	1	Biopsy
TGA (completed) + HLHS	25	1	Biopsy
TGA (completed)	24	2	Biopsy
TGA (completed) + PAS + VSD	26	1	Biopsy
TGA (corrected)	28	1	Biopsy
PTA + VSD	15	1	Biopsy
PTA + SASV	16	1	Biopsy
PTA + VSD	28	1	Biopsy
PTA + CH	12	1	Biopsy
HLHS + PSVC	35	1	Biopsy
HLHS + MA + TGA	25	1	Biopsy
HLHS + CoA + VSD	22	1	Biopsy
HLHS + DOVT + VSD	22	1	Biopsy
HLHS + TGA + PAS + MA	24	1	Biopsy
SASV	24	1	Biopsy
EFE	30	1	Biopsy
NVM	31	1	Biopsy
TA + VSD	25	1	Biopsy
TOF	22	1	Biopsy
TOF	25	1	Biopsy
TOF + VR	32	1	Biopsy
TOF + RAA	27	1	Biopsy
TOF + IIVC	25	1	Biopsy
MA + VSD	13	1	Biopsy
RAD	23	1	Biopsy
PAS + VSD	21	1	Biopsy
RVD	25	1	Biopsy
RVD + PA	31	1	Biopsy
CoA + VSD	21	1	Biopsy
RAA	27	2	Biopsy
Atrial myxoma	23	1	Biopsy
Rhabdomyoma of heart	29	1	Biopsy
Ebstein anomaly + VSD	26	1	Biopsy
Ebstein anomaly + effusion	32	1	Biopsy

APVC = anomalous pulmonary venous connection; CH = cystic hygroma; CoA = coarctation of aorta; DOVT = double outlet of right ventricle; ECD = endocardial cushion defect; EFE = endocardial fibroelastosis; HLHS = hypoplastic left heart syndrome; IIVC = interruption of inferior vena cava; MA = mitral atresia; NVM = noncompaction ventricular myocardium; PA = pulmonary atresia; PAS = pulmonary artery stenosis; PSVC = persistent left superior vena cava; PTA = persistent truncus arteriosus; RAA = right aortic arch; RAD = diverticulum of right atrium; RVD = right ventricular dysplasia; SASV = single atrium and single ventricle; TA = tricuspid atresia; TGA = transposition of the great arteries; TOF = tetralogy of Fallot; VR = vascular ring; VSD = ventricular septal defect.