

Original Article

Prenatal diagnosis of fetal gastroschisis using three-dimensional ultrasound: Comparison between the 20th and 21st centuries

Hsing-Fen Tsai^a, Yueh-Chin Cheng^a, Huei-Chen Ko^{b,c}, Lin Kang^a, Pei-Yin Tsai^a,
Chen-Hsiang Yu^a, Chiung-Hsin Chang^{a,*}, Fong-Ming Chang^{a,*}

^a Department of Obstetrics and Gynecology, National Cheng Kung University College of Medicine and National Cheng Kung University Hospital, Tainan, Taiwan

^b Department of Psychology, Asia University, Taichung, Taiwan

^c Institute of Behavior, Cheng Kung University College of Medicine, Tainan, Taiwan

Accepted 31 January 2013

Abstract

Objective: In order to compare the trends and improvements of prenatal diagnosis of gastroschisis, we herein retrospectively reviewed our cases of fetal gastroschisis detected by three-dimensional ultrasound (3D US) between the two centuries.

Materials and Methods: We reviewed our computer database of prenatal diagnosis on gastroschisis in National Cheng Kung University Hospital from October 1994 to November 2011. All the fetuses were initially scanned by two-dimensional (2D) US to locate the region of interest (ROI). Then, the 3D probe was used to scan all the ROI systematically and mechanically, and all the images were stored on laser discs for further 3D visualization and reconstruction. To compare the characteristics at prenatal diagnosis of gastroschisis between the 20th and 21st centuries in our hospital, the Chi-square test and Student *t* test were used. The *p* values less than 0.05 and 0.1 were considered statistically significant.

Results: In total, 26 fetuses with gastroschisis were depicted by 3D US *in utero* (10 cases were diagnosed in the 20th century and 16 cases in the 21st century). The ranges of gestational age at prenatal diagnosis of gastroschisis by 3D US in the 20th century were between 14 and 34 weeks (mean: 21.6 weeks) and between 14 and 33 weeks (mean: 21.9 weeks) in the 21st century. Moreover, seven cases (70%) were diagnosed before the third trimester in the 20th century, whereas 13 cases (81%) were diagnosed before the third trimester in the 21st century.

Conclusion: Although without statistical significance, higher prenatal diagnosis rate before the third trimester in the 21st century was noted. The improvement of 3D US has remarkable advantages in adding novel visual depiction of a 3D lesion of a 3D fetus in 3D US after reconstruction and thus assists substantially in prenatal diagnosis, genetic consultation, and perinatal management of gastroschisis.

Copyright © 2013, Taiwan Association of Obstetrics & Gynecology. Published by Elsevier Taiwan LLC. All rights reserved.

Keywords: gastroschisis; prenatal diagnosis; three-dimensional ultrasound

Introduction

Gastroschisis is one of the most important types of congenital abdominal wall defects. The incidence is about 1–5 per 10,000 births. Gastroschisis is typically located on the right side of a normally inserted umbilical cord with viscera

protrusion. Differential diagnosis of congenital abdominal wall defects should be performed precisely during ultrasonographic examination. Gastroschisis is generally considered as having a low rate of concurrent primary malformations and is not a significant component of major chromosomal or genetic syndrome. In contrast, omphalocele consists of a herniated sac with visceral contents and is associated with chromosomal anomalies. Notably, the prognosis of omphalocele is worse than that of gastroschisis [1–6].

The overall survival rate of gastroschisis ranges from 85% to 97%. The most frequent anomalies associated with gastroschisis are orofacial and gastrointestinal defects, followed by

* Corresponding authors. Department of Obstetrics and Gynecology, National Cheng Kung University Medical College and Hospital, 138 Victory Road, Tainan 70428, Taiwan.

E-mail addresses: ahsin@mail.ncku.edu.tw (C.-H. Chang), fchang@mail.ncku.edu.tw (F.-M. Chang).

neural tube defects and genitourinary malformations. Moreover, the related morbidity and mortality mainly depend on associated bowel complications. Several prenatal ultrasound (US) markers such as small for gestational age, extra-abdominal bowel dilatation, intra-abdominal bowel dilatation, stomach dilatation, stomach herniation, and thickened bowel wall are considered potentially related to adverse outcome in fetuses with gastroschisis. Furthermore, the strongest US marker predictive of complex gastroschisis is intra-abdominal bowel dilatation. Gastroschisis with complex defects including intestinal atresia, perforations, necrosis and volvulus are more likely to require extensive hospital resources and have poorer survival [7–9].

To date, three-dimensional US (3D US) has been applied in many fields and is helpful in diagnosing congenital anomalies *in utero*, although two-dimensional (2D) US is superior to 3D US for detection of contents within the viscera protrusion. However, 3D US can provide images with improved clarity, definition, and resolution, along with the increased probability of detecting additional subtle malformations that are not easily detectable on 2D US. These benefits make 3D US a valuable addition for the evaluation of fetuses with abdominal wall defects and have advantages in explaining the anomalies to the families involved, as well as genetic consultation [10–21]. In order to compare the trends and improvements of prenatal diagnosis of gastroschisis, we herein retrospectively reviewed our computer database of fetal gastroschisis detected by 3D US from October 1994 to November 2011.

Materials and methods

Patients and setting

From October 1994 to November 2011, the records of patients with fetal gastroschisis by 3D US were reviewed. In general, the patients were referred from local practitioners or from the Antenatal Care Clinic of National Cheng Kung University Hospital. The setting was at the Prenatal Ultrasound Lab of Department of Obstetrics and Gynecology, National Cheng Kung University Hospital, which is the largest national tertiary medical center in Southern Taiwan. All the

fetuses were followed to the end of pregnancy to confirm the diagnosis of gastroschisis. The informed consents were given by the patients. The study was approved by the Institutional Review of Board, National Cheng Kung University Hospital (IRB, ER-99-011).

Equipment

We used conventional 3D US scanners for prenatal screening. The 3D US machines were Voluson 530D (Kretz, Zipf, Austria), or Voluson 730 Expert (GE, Milwaukee, WI, USA) and Accuvix V20 (Medison, Seoul, Korea). The details of 3D US scanning have been described elsewhere [10–21]. In brief, the fetus with gastroschisis was initially scanned by 2D US to locate the region of interest (ROI). Then, the 3D probe was used to scan all the ROI systematically and mechanically, and all the images were stored in the laser discs for further 3D visualization and reconstruction. Subsequently, the 3D images were demonstrated on the screen. First, the multiplanar orthogonal view was illustrated. Second, reconstructions of various modes were depicted, including surface-rendering mode, transparent mode, and maximal intensity mode.

Statistics

In order to compare the gestational age at prenatal diagnosis of gastroschisis between the 20th and 21st centuries in National Cheng Kung University Hospital, Chi-square test and Student *t* test were undertaken. The *p* values less than 0.05 and 0.1 were considered statistically significant.

Results

During the study period between October 1994 and November 2011, in total, 26 fetuses with gastroschisis were depicted by 3D US *in utero* (Tables 1 and 2). Table 1 shows the cases (total 10 cases) diagnosed before January 2000, and Table 2 lists the cases (total 16 cases) diagnosed from January 2000 to November 2011. The ranges of gestational age at prenatal diagnosis of gastroschisis by 3D US in the 20th century were between 14 and 34 weeks (mean: 21.6 weeks)

Table 1
Prenatal diagnosis of fetal gastroschisis (GS) using 3D US in the 20th century.

Case no.	Maternal age (y)	Pregnancy history	Gestational age (wk)	US diagnosis	Outcome	Karyotype	Associated conditions
1	28	G2P1	14	GS	TOP	ND	—
2	20	G1P0	14	GS	C/S	46, XX	—
3	22	G1P0	16	GS	Follow-up	ND	—
4	29	G1P0	16	GS	Follow-up	ND	—
5	29	G1P0	17	GS	TOP	ND	Pleural effusion Pericardial effusion
6	20	G3P0A2	20	GS	C/S	ND	—
7	18	G1P0	23	GS	Follow-up	ND	—
8	31	G3P2	28	GS	Follow-up	ND	—
9	24	G1P0	34	GS	C/S	46, XX	SGA Oligohydramnios
10	16	G1P0	34	GS	VD	ND	SGA

3D US = three-dimensional ultrasound; C/S = cesarean section; Follow-up = Follow-up at outside clinics; ND = not done; SGA = small for gestational age; TOP = termination of pregnancy; VD = vaginal delivery.

Table 2
Prenatal diagnosis of fetal gastroschisis (GS) using 3D US in the 21st century.

Case no.	Maternal age (y)	Pregnancy history	Gestational age (wk)	US diagnosis	Outcome	Karyotype	Associated conditions
1	20	G1P0	14	GS	Follow-up	46, XX	—
2	23	G2P1	15	GS	Follow-up	ND	—
3	24	G1P0	17	GS	Follow-up	ND	—
4	23	G1P0	18	GS	Follow-up	ND	EIF
5	23	G1P0	18	GS	Follow-up	ND	—
6	29	G1P0	20	GS	TOP	ND	SGA SUA
7	29	G3P2	20	GS	PTL	ND	—
8	24	G1P0	21	GS	Follow-up	ND	—
9	26	G1P0	21	GS	Follow-up	46, XX	—
10	20	G1P0	21	GS	C/S	ND	EIF
11	22	G1P0	22	GS	Follow-up	46, XY	—
12	24	G3P2	24	GS	C/S	46, XX	—
13	16	G1P0	26	GS	TOP	ND	SGA
14	39	G3P2	30	GS	C/S	ND	SGA Pyelectasis
15	25	G1P0	31	GS	C/S	ND	SGA Oligohydramnios
16	21	G1P0	33	GS	Follow-up	ND	—

3D US = three-dimensional ultrasound; C/S = cesarean section; EIF = echogenic intracardiac focus; Follow-up = Follow-up at outside clinics; ND = not done; PTL: preterm labor; SGA = small for gestational age; SUA = single umbilical artery; TOP: termination of pregnancy.

and between 14 and 33 weeks (mean: 21.9 weeks) in the 21st century. Notably, seven cases (70%) were diagnosed before the third trimester in the 20th century, but 13 cases (81%) were diagnosed before the third trimester in the 21st century.

Furthermore, a total of nine cases were complicated with other additional abnormalities. As listed in Table 1, three cases (30%) in the 20th century with associated anomalies were as follows: small for gestational age (2 cases), pericardial effusion (1 case), pleural effusion (1 case), and oligohydramnios (1 case). As listed in Table 2, six cases (38%) in the 21st century with associated anomalies are as follows: small for gestational age (4 cases), echogenic intracardiac focus (2 cases), oligohydramnios (1 case), single umbilical artery (1 case), and pyelectasis (1 case). Moreover, in all the six fetuses with karyotyping, none had chromosomal abnormalities.

Both the accuracy rate of prenatal diagnosis of gastroschisis by 2D and 3D US were 100%, but 3D US can provide additional illustrations in 3D after various modes of reconstruction, thereby depicting additional abnormalities more easily. Nevertheless, the images of 3D US can reveal three orthogonal planes, including coronal, sagittal, and axial views, of a fetus with gastroschisis that allow the parents to have a better understanding of the fetal malformation. Besides, the additional illustrations in 3D US can reduce the discrepancy in decision making and prenatal consultation between patients and obstetricians (Figs. 1 and 2).

As shown in Table 3, in both the 20th and 21st centuries, most of the cases were diagnosed before the third trimester (seven cases in the 20th century, and 13 cases in the 21st century). The mean gestational age at prenatal diagnosis of gastroschisis in the 21st century was 21.9 weeks of gestation (SD: 5.58 weeks), while the mean gestational age in the 20th century was 21.6 weeks of gestation (SD: 7.83 weeks). The Chi-square test was used for testing the frequencies of the

gestational age at diagnosis between the two centuries using 28 weeks of gestation as the cut-off point. The Student *t* test was applied for testing the differences of the mean gestational age at diagnosis between the two centuries. The trend analysis did not show that the gestational age at the prenatal diagnosis of gastroschisis in the 21st century was significantly different from that in the 20th century ($p = 0.508$ by the Chi-square test, $p = 0.453$ by the Student *t* test).

Discussion

Comparison of gestational age at prenatal diagnosis

With the development of clinical use and improvement of reconstruction technology in 3D US over the past decade, we



Fig. 1. Prenatal 2D ultrasound of gastroschisis at 20 weeks of gestation with viscera protrusion (arrow).

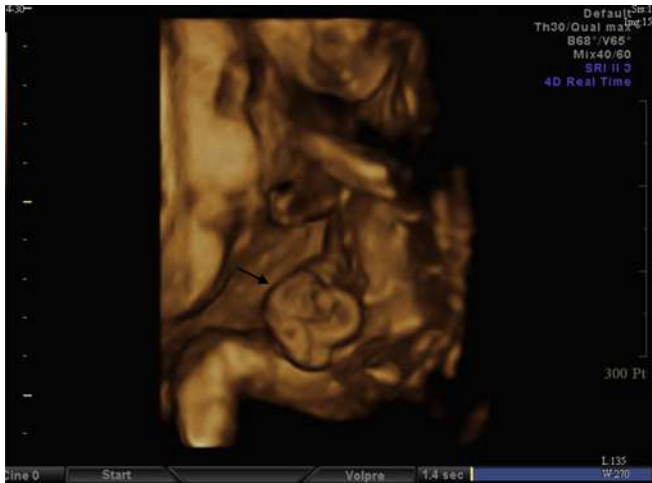


Fig. 2. Prenatal 3D ultrasound (surface rendering mode) of gastroschisis at 20 weeks of gestation (the same case as Fig. 1) with viscera protrusion (arrow).

investigate if there are any differences in timing and accuracy of diagnosis of fetal gastroschisis by 3D US between the centuries. Therefore, we compared the cases of gastroschisis in the 20th century with those in the 21st century (Table 3), and the results showed no difference in the gestational age at prenatal diagnosis of gastroschisis between the 20th and 21st centuries ($p = 0.508$ by Chi-square test, $p = 0.453$ by Student t test). This result may be owing to the small number of cases (total 26 cases). Although without statistical significance, a higher prenatal diagnosis rate before the third trimester in the 21st century was noted (70% in the 20th century, and 81% in the 21st century). The possible reasons for the phenomenon of higher prenatal diagnosis rate of gastroschisis may be owing to the improvement of 3D US machines and the improved technique, as well as elevated awareness of physicians. 3D US has advantages in adding novel visual depiction of a 3D lesion of a 3D fetus in 3D US after reconstruction, thereby assisting substantially in prenatal consultation and genetic screening [10–21].

Comparison of maternal age

In the 20th century, no case (0%) had advanced maternal age, while one case (6%) with advanced maternal age was observed in the 21st century. In the 20th century, the mean maternal age of those with fetal gastroschisis was 23.7 years, while it was 24.3 years in the 21st century. From these comparisons, it was found that the maternal age did not change significantly between the two centuries.

Comparison of associated anomalies

Gastroschisis is generally accepted as having a low rate of concurrent primary malformations and is not a significant component of major chromosomal or genetic syndrome. Furthermore, the most frequent anomalies associated with gastroschisis are orofacial and gastrointestinal defects, followed by neural tube defects and genitourinary malformations [7–9]. In our series, three cases (30%) in the 20th century were complicated with other associated abnormalities, including small for gestational age (2 cases), pericardial effusion (1 case), pleural effusion (1 case), and oligohydramnios (1 case). In the 21st century, six cases (38%) were complicated with other abnormalities, namely, small for gestational age (4 cases), echogenic intracardiac focus (2 cases), oligohydramnios (1 case), single umbilical artery (1 case), and pyelectasis (1 case). Moreover, in all the six fetuses with karyotyping, none had chromosomal abnormalities. From these comparisons, the incidence of associated anomalies did not change significantly between the two centuries.

Associated anomalies and fetal outcome

On prenatal consultation of the prognosis of gastroschisis, the presence of associated anomalies may be accompanied with worse outcomes, such as higher perinatal death rates and postnatal morbidities. Fetal intra-abdominal bowel dilatation depicted by US would be related with complex defects, including intestinal atresia, perforations, necrosis, and volvulus, and they more likely require extensive hospital resources and have poorer survival [7–9]. Therefore, it is very important for prenatal consultation to precisely depict fetal gastroschisis with or without associated anomalies, abnormal karyotyping, as well as to predict fetal prognosis.

Molecular genetics and 3D US

Furthermore, recent advances of molecular diagnosis have contributed remarkably to fetal medicine and genetic consultation [22–30]. Novel research modalities, such as array comparative genomic hybridization characterization, and molecular cytogenetic analysis, in conjunction with 3D US should be undertaken altogether to reach the new horizon in prenatal diagnosis, genetic consultation, as well as perinatal management of fetal gastroschisis [22–30].

Table 3

Comparison of gestational age (GA) at diagnosis of fetal gastroschisis by 3D US.

	Mean maternal age (y)	GA before the third trimester (<28 wk)*	GA at the third trimester (≥28 wk)**	Total no. of cases
20 th century (1994–2000)	23.7	7 (70%)	3 (30%)	10 (100%)
21 st century (2000–2011)	24.3	13 (81%)	3 (19%)	16 (100%)

* $p = 0.508$ (nonsignificant) by Chi-square test for testing the frequencies of the gestational age at diagnosis between the two centuries using the 28 weeks of gestation as the cut-off.

** $p = 0.453$ (nonsignificant) by Student t test for testing the differences of the mean gestational age at diagnosis between the two centuries.

Conclusion

In conclusion, although without statistical significance, higher prenatal diagnosis rate before the third trimester in 21st century was noted. Over the past decades, we have engaged in the development of clinical use of 3D US in fetal medicine [10–20, 31–37]. From this series, we further prove that 3D US can be applied in antenatal diagnosis of fetal congenital anomaly, and thus has substantial advantages in clinical medicine.

Acknowledgments

We are grateful to the staff of the Prenatal Ultrasound Lab of Department of Obstetrics and Gynecology, National Cheng Kung University Hospital. This series was supported in part by a grant from National Science Council, Executive Yuan, Taipei, Taiwan.

References

- [1] Baird PA, McDonald EC. An epidemiologic study of congenital malformations of the anterior abdominal wall in more than half a million consecutive births. *Am J Human Genet* 1981;34:470–2.
- [2] Calzolari E, Bianchi F, Dolk H, Milan M. Omphalocele and gastroschisis in Europe: a survey of 3 million births 1980–1990. *Am J Med Genet* 1995;58:187–94.
- [3] Bonilla-Musoles F, Machado LE, Bailão LA, Osborne NG, Raga F. Abdominal wall defects: two- versus three-dimensional ultrasonographic diagnosis. *J Ultrasound Med* 2001;20:379–89.
- [4] Wilson RD, Johnson MP. Congenital abdominal wall defects: An update. *Fetal Diagn Ther* 2004;19:385–98.
- [5] Mastroiacovo P, Lisi A, Castilla EE. The incidence of gastroschisis: research urgently needs resources. *BMJ* 2006;332:423–4.
- [6] Ruano R, Picone O, Bernardes L, Martinovici J, Dumez Y, Benachi A. The association of gastroschisis with other congenital anomalies: how important is it? *Prenat Diagn* 2011;31:347–50.
- [7] Luton D, De Lagausie P, Guibourdenche J, Oury JF, Vuillard E, Sibony O, et al. Prognostic factors of prenatally diagnosed gastroschisis. *Fetal Diagn Ther* 1997;12:7–14.
- [8] Snyder CL. Outcome analysis for gastroschisis. *J Pediatr Surg* 1999;34:1253–6.
- [9] Kuleva M, Khen-Dunlop N, Dumez Y, Ville Y, Salomon LJ. Is complex gastroschisis predictable by prenatal ultrasound? *BJOG* 2012;119:102–9.
- [10] Lai TH, Chang CH, Yu CH, Kuo PL, Chang FM. Prenatal diagnosis of alobar holoprosencephaly by two-dimensional and three-dimensional ultrasound. *Prenat Diagn* 2000;20:400–3.
- [11] Chuang L, Chang CH, Yu CH, Chang FM. Three-dimensional sonographic visualization of a fetal omphalocele at 14 weeks of gestation. *Prenat Diagn* 2000;20:523–4.
- [12] Bega G, Lev-Toaff A, Kuhlman K, Kurtz A, Goldberg B, Wapner R. Three-dimensional ultrasonographic imaging in obstetrics: present and future applications. *J Ultrasound Med* 2001;20:391–408.
- [13] Pretorius DH, Nelson TR. Fetal three-dimensional ultrasonography: today or tomorrow. *J Ultrasound Med* 2001;20:283–6.
- [14] Shih JC, Chen CP, Hsieh FJ. Three-dimensional ultrasonography in genetic screening and counseling. *Ultrasound Rev Obstet Gynecol* 2001;1:120–7.
- [15] Kang L, Chang CH, Yu CH, Chang FM. Prenatal depiction of cystic hygroma using three-dimensional ultrasound. *Ultrasound Med Biol* 2002;28:719–23.
- [16] Chang CH, Chang FM, Yu CH, Liang RI, Ko HC, Chen HY. Systemic assessment of fetal hemodynamics by Doppler ultrasound. *Ultrasound Med Biol* 2000;26:777–85.
- [17] Chang CH, Chang FM, Yu CH, Liang RI, Ko HC, Chen HY. Fetal ear assessment and prenatal detection of aneuploidy by the quantitative three-dimensional ultrasonography. *Ultrasound Med Biol* 2000;26:743–9.
- [18] Merz E. 3-D ultrasound in prenatal diagnosis. *Curr Obstet Gynecol* 1999;9:93–100.
- [19] Wang P, Chang FM, Chang CH, Yu CH, Jung YC, Huang CC. Prenatal diagnosis of Joubert syndrome complicated with encephalocele using two-dimensional and three-dimensional ultrasound. *Ultrasound Obstet Gynecol* 1999;14:360–2.
- [20] Lin HH, Liang RI, Chang FM, Chang CH, Yu CH, Yang HB. Prenatal diagnosis of otocephaly using two-dimensional and three-dimensional ultrasonography. *Ultrasound Obstet Gynecol* 1998;11:361–3.
- [21] Merz E, Bahlmann F, Weber G, Macchiella D. Three-dimensional ultrasonography in prenatal diagnosis. *J Perinat Med* 1995;23:213–22.
- [22] Chen CP, Su YN, Chern SR, Wu PS, Su JW, Town DD, et al. Prenatal diagnosis of an interstitial deletion of 10q (10q11.21→q21.1): array comparative genomic hybridization characterization and literature review. *Taiwan J Obstet Gynecol* 2012;51:672–6.
- [23] Hsu PY, Yu CH, Lin K, Cheng YC, Chang CH, Chang FM. Prenatal diagnosis of fetal multicystic dysplastic kidney in the era of three-dimensional ultrasound: 10-year experience. *Taiwan J Obstet Gynecol* 2012;51:596–602.
- [24] Tsai PY, Chang CH, Yu CH, Cheng YC, Chang FM. Three-dimensional ultrasound in the prenatal diagnosis of osteogenesis imperfecta. *Taiwan J Obstet Gynecol* 2012;51:387–92.
- [25] Chen CP, Huang HK, Ling PY, Su YN, Chen M, Tsai FJ, et al. A de novo duplication of chromosome 21q22.11→qter associated with Down syndrome: prenatal diagnosis, molecular cytogenetic characterization and fetal ultrasound findings. *Taiwan J Obstet Gynecol* 2011;50:492–8.
- [26] Chen CP, Su YN, Chen YY, Chern SR, Liu YP, Wu PC, et al. Chromosome 1p32-p31 deletion syndrome: prenatal diagnosis by array comparative genomic hybridization using uncultured amniocytes and association with NFIA haploinsufficiency, ventriculomegaly, corpus callosum hypogenesis, abnormal external genitalia, and intrauterine growth restriction. *Taiwan J Obstet Gynecol* 2011;50:345–52.
- [27] Chen CP, Ko TM, Su YN, Chern SR, Su JW, Chen YT, et al. Prenatal diagnosis of mosaic tetrasomy 18p. *Taiwan J Obstet Gynecol* 2012;51:625–9.
- [28] Chen CP, Chern SR, Chen YY, Wu PC, Town DD, Chen WL, et al. Monozygotic twins with trisomy 18 of paternal origin: prenatal diagnosis and molecular cytogenetic characterization in a pregnancy with one structurally abnormal living fetus and one intrauterine fetal demise. *Taiwan J Obstet Gynecol* 2012;51:430–4.
- [29] Chen CP. Prenatal findings and the genetic diagnosis of fetal overgrowth disorders: Simpson-Golabi-Beckwith syndrome, Sotos syndrome, and Beckwith-Wiedemann syndrome. *Taiwan J Obstet Gynecol* 2012;51:186–91.
- [30] Chen CP, Su YN, Chang CL, Chen YY, Su JW, Chern SR, et al. Rapid aneuploidy diagnosis by multiplex ligation-dependent probe amplification using uncultured amniocytes in pregnancy with major fetal structural abnormalities. *Taiwan J Obstet Gynecol* 2012;51:123–8.
- [31] Wu MH, Cheng YC, Chang CH, Ko HC, Chang FM. Three-dimensional ultrasound in evaluation of the ovary. *J Med Ultrasound* 2012;20:136–41.
- [32] Lee IW, Chang CH, Cheng YC, Ko HC, Chang FM. A review of three-dimensional ultrasound applications in fetal growth restriction. *J Med Ultrasound* 2012;20:142–9.
- [33] Liao SL, Tsai PY, Cheng YC, Chang CH, Ko HC, Chang FM. Prenatal diagnosis of fetal encephalocele using three-dimensional ultrasound. *J Med Ultrasound* 2012;20:150–4.
- [34] Tsai HF, Kang L, Tsai PY, Cheng YC, Chang CH, Ko HC, et al. Prenatal diagnosis of fetal cystic hygroma using three-dimensional ultrasound in 2000–2011. *J Med Ultrasound* 2012;20:155–61.
- [35] Bai YR, Tsai PY, Cheng YC, Chang CH, Chang FM. Prenatal diagnosis of fetal schizencephaly by ultrasonography and magnetic resonance imaging. *J Med Ultrasound* 2012;20:162–8.
- [36] Wu PY, Hsu KF, Chang CH, Chang FM. Ultrasonographic diagnosis and treatment of a giant uterine cervical Nabothian cyst. *J Med Ultrasound* 2012;20:169–72.
- [37] Chang FM, Chang CH, Ko HC. Three-dimensional ultrasound in prenatal diagnosis and reproductive medicine. *J Med Ultrasound* 2012;20:133–5.