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Novel application of 4D sonography with B-flow imaging and spatio-temporal image correlation (STIC) in the assessment of the anatomy of pulmonary arteries in fetuses with pulmonary atresia and ventricular septal defect

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KEYWORDS: 3D/4D ultrasound; echocardiography; fetal heart defect; pulmonary atresia; ventricular septal defect

ABSTRACT

Objectives *To assess the reliability of two-dimensional gray-scale (2D) and color Doppler echocardiography in the study of the size and anatomy of the central pulmonary arteries and of the sources of pulmonary blood flow in a case series of fetuses with pulmonary atresia and ventricular septal defect (PA-VSD), and to evaluate whether the use of 4D ultrasound with B-flow imaging and spatio-temporal image correlation (STIC) can improve prenatal diagnostic accuracy.*

Methods *The study population comprised a group of seven PA-VSD fetuses that had been examined by 2D and color Doppler echocardiography exclusively, and a group of five additional cases identified initially by conventional echocardiography and examined further by 4D ultrasound, for all of which a thorough postnatal or autopsy study of the size and anatomy of the pulmonary arteries and blood supply was available.*

Results *2D and color Doppler echocardiography failed to assess the anatomy of the central pulmonary arteries and the source of the pulmonary blood supply in 33% and 25% of the 12 cases, respectively. 4D ultrasound with B-flow imaging and STIC assessed successfully the anatomy of the pulmonary arteries and the source of pulmonary blood supply in all five fetuses examined.*

Conclusions *The prognosis of PA-VSD is influenced by the anatomy of the pulmonary arteries and the sources of the pulmonary blood supply, and by coexisting extracardiac and genetic anomalies. Our findings, although limited to a small sample size, suggest that 4D echocardiography with B-flow imaging and STIC, unlike 2D ultrasound, can provide thorough visualization of very small vessels and of the arterial blood supply to the lungs of fetuses with PA-VSD. 4D ultrasound may be used in the future to improve and help to detail the diagnosis of other fetal cardiac defects. Copyright © 2006 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Pulmonary atresia with ventricular septal defect (PA-VSD) is a rare and severe congenital heart defect characterized by a complete obstruction, or absence of communication, between the right ventricle and the pulmonary artery[1–3]. The pulmonary trunk is usually involved; in extreme cases it can be completely absent. When the right and left pulmonary arteries (RPA and LPA) are present, they are commonly smaller than normal and confluent, with the characteristic appearance of a 'flying seagull'[4] (Figure 1a). Their size is usually dependent on the source of arterial supply. The pulmonary vascular bed may be supplied with blood from the ductus arteriosus (DA), from major aortopulmonary collateral arteries (MAPCA), or from a combination of both[3,5].

Along with the presence of extracardiac and genetic anomalies[6–10], the prognosis of PA-VSD is influenced by the anatomy of the pulmonary arteries and by the sources of pulmonary blood supply[11,12], whose appreciation helps to provide fully informed prenatal counseling.

Based on the analysis of large series of fetuses with heart defects[13,14] two-dimensional gray-scale (2D)

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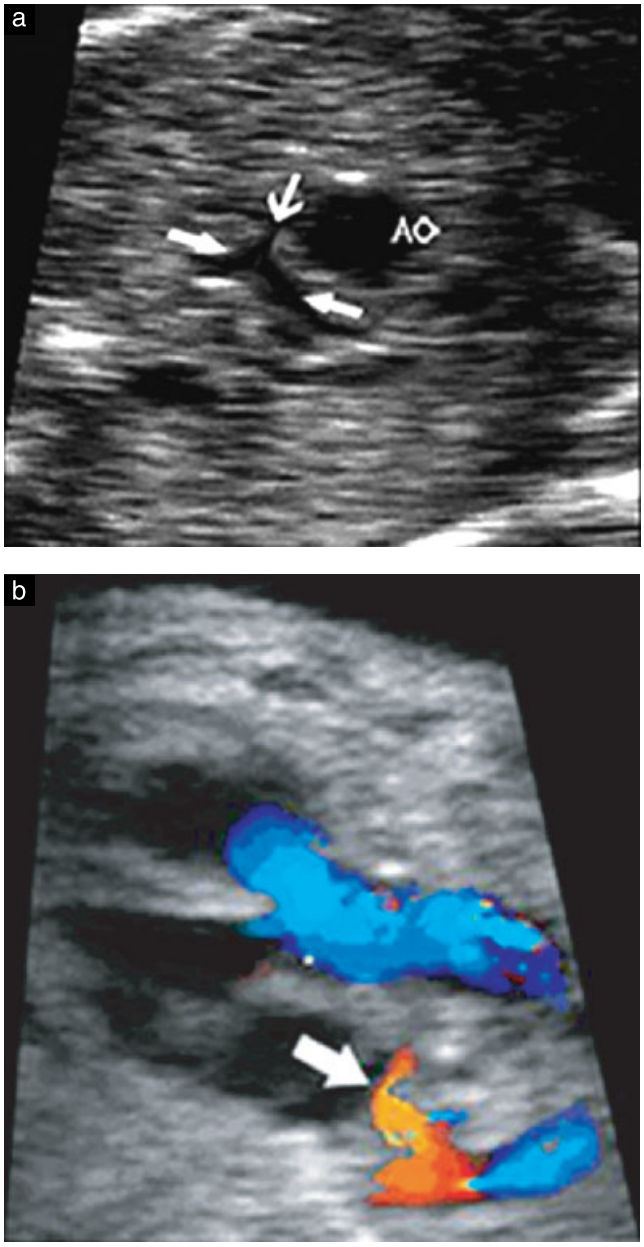

Figure 1 (a) Cross-sectional view of the fetal thorax, at the level of the great arteries, showing the 'flying seagull' appearance of the branch pulmonary arteries (thick arrows). The main pulmonary artery stops before reaching the outflow tract (thin arrow). AO, aorta. (b) Color Doppler showing one major aortopulmonary collateral artery (arrow) arising from the descending aorta.

echocardiography appears to identify reliably cases of PA-VSD. In contrast, the accuracy of 2D and color Doppler echocardiography to assess the size and confluence of the pulmonary arteries and the source of the pulmonary blood supply has been evaluated only in postnatal series of patients with PA-VSD[15,16], and data on prenatal examination are lacking.

B-flow imaging is a new technique that uses digitally encoded sonographic technology to provide direct visualization of blood echoes in gray scale. It displays simultaneously both tissue morphology and blood flow using the same gray-scale schemes (unlike color Doppler flow, in which the color signals are superimposed onto structural gray-scale images)[17–19]. The B-flow image does not interfere with the information produced by B-mode because both utilize the same spatial resolution and frame rate. When compared with color and power Doppler sonography, B-flow sonography has a higher frame rate and better spatial resolution. It allows angle-independent detection of weak blood reflectors from vessels[17–19]. Moreover, it has been suggested to allow better visualization of small vessels with low flow velocity[20,21].

The aim of this study was two-fold: first, to estimate the ability of 2D and color Doppler echocardiography to assess the size and anatomy of the central pulmonary arteries and to identify the sources of pulmonary blood flow in a case series of fetuses with PA-VSD; second, to compare 2D echocardiography and 4D ultrasound with B-flow imaging and spatio-temporal image correlation (STIC), in an attempt to clarify whether the latter approach might add diagnostic information to better define the prognosis of fetuses with PA-VSD.

METHODS

To assess the accuracy of fetal 2D echocardiography in identifying the sources of pulmonary blood flow and the anatomy of the pulmonary arteries, we first conducted a retrospective study of all cases that had been diagnosed with PA-VSD at our center in the period 1994–2003, and for which postnatal echocardiography and/or an autopsy report was available. Fetuses with PA-VSD and additional major heart defects were not included. Overall, we retrieved nine cases, but two were excluded due to the lack of an autopsy report. In all cases, fetal 2D echocardiography had been performed with an ultrasound system provided with pulsed, continuous and color Doppler (Prosound 5000 Aloka, Tokyo, Japan).

Then, we sought to evaluate whether the use of 4D ultrasound would improve the prenatal assessment of PA-VSD. With this aim, starting from January 2004, all cases diagnosed as PA-VSD at 2D and color Doppler echocardiography were examined further by 4D ultrasound with B-flow imaging and STIC, using a Voluson 730 Expert ultrasound machine (General Electric Medical Systems, Kretztechnik, Zipf, Austria). Again, fetuses with additional major heart defects were not included. In this way, we were able to study a further five fetuses.

In all cases, the size and anatomy of the pulmonary arteries and the nature of the blood supply to the lungs were established conclusively by catheterization and angiography, and/or at surgery or autopsy.

The following quantitative echocardiographic parameters were retrieved from recorded videotapes and/or measured on an offline computer and analyzed: cardiothoracic ratio and maximum diameter of pulmonary branches. These measurements were compared with established normal sizes[22,23]. The diameters of the LPA and RPA were measured from 2D images in a short-axis view of the right ventricular outflow tract or in a three-vessels

view. These views were also used to determine the presence or absence of a main pulmonary artery and to document LPA-to-RPA direct continuity. We identified the side on which the aortic arch was using the three vessels and trachea view. MAPCA were defined as vessels connecting the descending aorta with pulmonary terminations either at the distal branch of the pulmonary arteries or within the lung parenchyma (Figures 1b and 2); less frequently, individual collateral arteries can also originate from the brachiocephalic arteries or even from the coronary arteries. Commonly they are between two and six in number.

DA was defined as a vessel connecting the undersurface of the aortic isthmus with the pulmonary artery bifurcation. When retrograde flow from the transverse aortic arch or from the end of the arch was demonstrated, the source of the pulmonary arteries was considered to be the DA; when retrograde flow originated from the descending aorta or from aortic arch branches, the source of the pulmonary blood supply was considered to be the MAPCA.

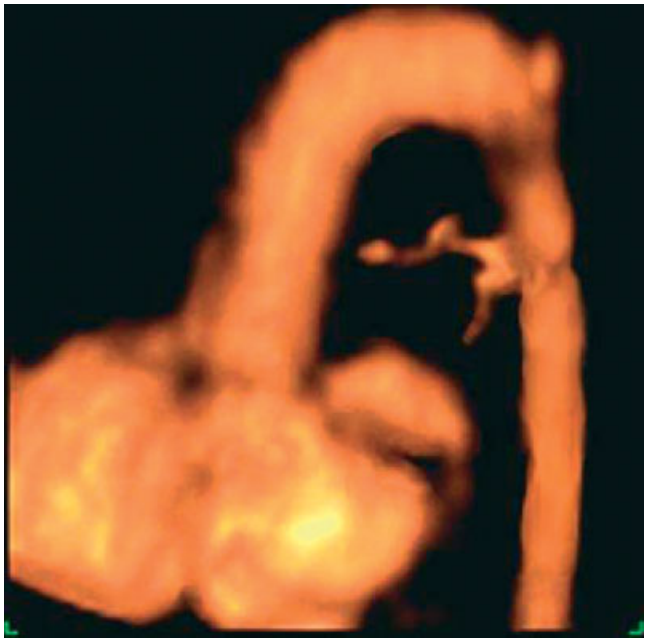

Figure 2 Three-dimensional sonography with B-flow imaging of the aortic arch and descending aorta, showing two major aortopulmonary collateral arteries arising from the thoracic aorta.

In the second part of the study, after 2D and color Doppler evaluation of each case, once the apical four-chamber view of the heart was visualized, heart volume datasets were acquired with B-flow imaging and STIC using transverse sweeps through the fetal thorax. B-flow settings during acquisition were: sensitivity = 4 and persistence = 2. The time acquisition lasted between 7.5 and 12.5 s and the acquisition angle varied from 20° to 30°. Volume datasets were displayed initially using multiplanar slicing. The original plane of acquisition, containing the apical four-chamber view of the heart, was displayed in Panel A of the screen; a transverse orthogonal view of the heart was displayed in Panel B and a coronal orthogonal view in Panel C. Then volume rendering was applied to the dataset, and a 3D image with the same orientation as that in Panel A was displayed in the lower right panel of the screen. The direction of view (green line on the left of the rendering box) was set with the same orientation as that in Panel A. The region of interest was adjusted on Panel B in an attempt to display a thick-slice rendering that comprised the fetal heart and its vascular connections, the aortic arch and the whole aortothoracic tract. Surface rendering was performed with a mixture of gradient light plus surface algorithms. Post-processing adjustments were performed as necessary, including gray-scale threshold and transparency, to improve image quality.

The rendered images were analyzed to evaluate the anatomy of the central pulmonary arteries and the source of the pulmonary blood supply. To obtain optimal images, the 4D images were frozen and the most informative volume dataset within the cardiac cycle was chosen.

Table 1 Sonographic characterization of pulmonary atresia with ventricular septal defect by two-dimensional gray-scale and color Doppler echocardiography

Case	*Gestational age (weeks)*	*Confluent pulmonary arteries*	*Source of pulmonary blood flow*	*Location of aortic arch*	*Postnatal/autopsy findings*	*Outcome*
1*	22	Yes	DA	Left	Confirmed	TOP
2	21	Yes	DA	Left	Confirmed	Alive
3	22	—	MAPCA	Right	Non-confluent PA	TOP
4	21	Yes	DA	Left	Confirmed	Alive
5	21	Yes	—	Right	DA	TOP
6	22	—	—	Right	Confluent PA and MAPCA	TOP
7	31	Yes	DA	Left	Confirmed	Alive
8	22	Yes	DA	Left	Confirmed	Alive
9	21	Yes	DA	Left	Confirmed	Alive
10	26	—	MAPCA	Right	Confluent PA	Alive
11	21	Yes	DA	Left	Confirmed	Alive
12	22	—	—	Right	Non-confluent PA and MAPCA	TOP

*This was the only case with associated cardiomegaly. —, not identified; DA, ductus arteriosus; MAPCA, major aortopulmonary collateral arteries; PA, pulmonary arteries; TOP, termination of pregnancy.

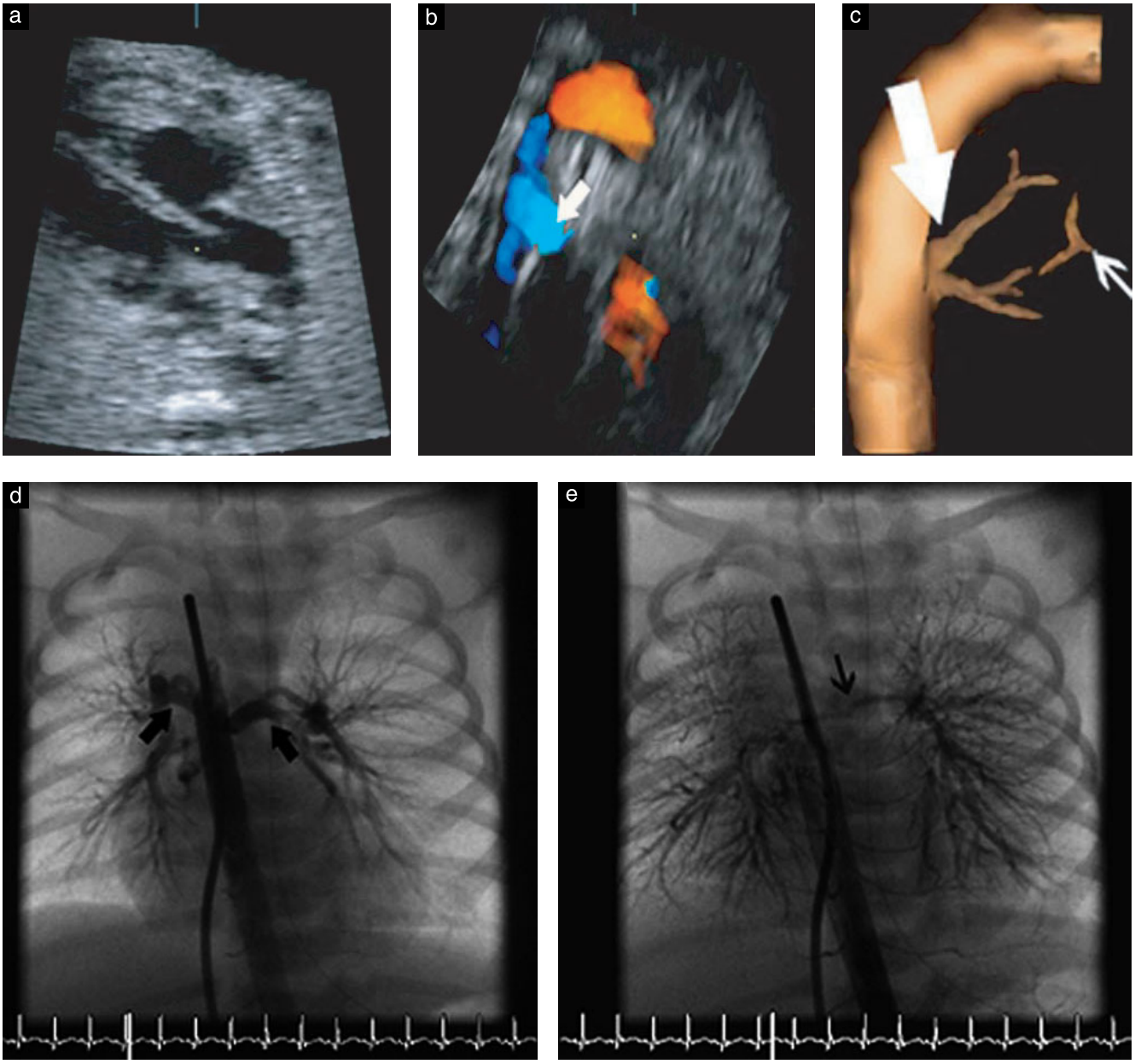

Figure 3 Case 10. Both pre- and postnatal echocardiography identified only the aortic outflow tract (a) and one major aortopulmonary collateral artery (MAPCA) arising by the descending aorta (b; arrow), with no evidence of confluent pulmonary arteries. This was instead demonstrated by B-flow with spatio-temporal image correlation (c), and confirmed by cardiac catheterization (d, e), along with the presence of a second MAPCA that had been missed on two-dimensional sonography. In (c) the large arrow indicates the MAPCA and the small arrow indicates the confluence of the pulmonary arteries. In (d) the arrows indicate the MAPCA. In (e) the arrow indicates the confluence of the pulmonary arteries.

RESULTS

We identified 14 fetuses with isolated PA-VSD among 910 cases of fetal heart defects at our center over a period of 12 years (1.54%). The mean gestational age at diagnosis was 23 (range, 21–31) weeks, with 10/14 cases diagnosed prior to 24 weeks of gestation.

Among the 12 cases with postnatal or autopsy confirmation, 2D and color Doppler echocardiography allowed us to identify eight fetuses with confluent central pulmonary arteries (Table 1). Cardiomegaly was present in one case (Case 1). The dimensions of the pulmonary arteries were, in all but two cases, at least 2 SDs below the mean value for gestational age; in the remaining two cases they were 1 SD below the mean. Assessment of the anatomy of the central pulmonary arteries was not possible in four patients (Cases 3, 6, 10 and 12). In two of these cases (Cases 6 and 10), hypoplastic central pulmonary arteries proved to be confluent at postnatal angiography or autopsy; in the other two they were non-confluent (Cases 3 and 12). At 2D and color Doppler echocardiography, the source of the pulmonary blood supply was identified correctly in 9/12 fetuses (MAPCA in two and DA in seven cases). In the remaining three fetuses, the pattern of pulmonary blood supply could

not be assessed reliably (Cases 5, 6 and 12) (Table 1). Overall, 2D and color Doppler echocardiography failed to evaluate the anatomy of the central pulmonary arteries in 33% of cases of PA-VSD and to assess the source of the pulmonary blood supply in 25% of them.

In contrast, 4D ultrasound with B-flow imaging and STIC assessed correctly the anatomy of the pulmonary arteries and the source of the pulmonary blood supply in all five of the fetuses with PA-VSD examined. Noteworthy, in one case (Case 10) both fetal 2D ultrasound and postnatal echocardiography failed to identify reliably the confluence of the pulmonary arteries, which was recognized by 4D ultrasound examination and confirmed definitively at the time of catheterization by angiography (Figure 3).

Right aortic arch was present in 5/12 cases and it was assessed correctly in all cases at 2D echocardiography.

DISCUSSION

This study, albeit comprising a relatively small cohort of fetuses with PA-VSD, suggests that 4D ultrasound with B-flow imaging and STIC is able to assess thoroughly the anatomy of the pulmonary arteries and the sources of pulmonary blood flow, supplying valuable information that cannot be obtained reliably by 2D fetal sonography.

Conventional fetal echocardiography appears to identify reliably cases of PA-VSD, as shown by large case series of fetuses with CHD[13,14,24], although, in some instances, the differential diagnosis from common arterial trunk may cause some difficulty[25]. However, assessment of the anatomy of the central pulmonary arteries and of the pattern of pulmonary blood flow is not always easy to define even at postnatal echocardiography[15,16].

Isolated PA-VSD presents a difficult management plan, since variations in blood supply to the pulmonary arterial tree may be complex and create significant variations in the development of the pulmonary arteries[1,3,26]. The presence of central pulmonary arteries of appropriate size and the relationship of the RPA and LPA are of surgical relevance. The central pulmonary arteries are considered 'confluent' when they maintain free communication with each other (Figure 1a). If all intrapulmonary arteries are connected to confluent pulmonary arteries, the pulmonary blood supply is said to be unifocal; commonly, in this case, the source of the pulmonary blood flow is the DA. When the lungs are supplied by more than one source, the pulmonary blood supply is said to be multifocal[3]. In this case confluent pulmonary arteries, themselves fed by one or more MAPCA, are connected to only a part of the lungs, while the remainder of the parenchyma is supplied directly by a variable number of MAPCA. Multifocal collateral blood supply is commonly associated with arborization abnormalities[3,26]. Indeed, the number of MAPCA turns out to correlate inversely with the completeness of arborization of the LPA and RPA.

Figure 4 represents schematically the main patterns of pulmonary arterial supply. The most favorable arrangement is that in which the RPA and LPA are confluent and are supplied by the DA[3]. In the second major pattern, the central pulmonary arteries are confluent and coexist with MAPCA. The third pattern is the complete absence of the central pulmonary arteries, the lungs being supplied directly by multiple MAPCA. This last pattern, associated with absent central pulmonary arteries, has the worst prognosis and is the most difficult to treat in postnatal life[3,12]. Hence, knowledge of all sources of pulmonary blood supply and the anatomy of the pulmonary arteries in cases of PA-VSD is essential for appropriate surgical planning, and to offer fully informed prenatal counseling to the couple.

This study emphasizes the difficulties of 2D and color Doppler echocardiography in the evaluation of the size and anatomy of the pulmonary arteries and in the assessment of the pulmonary blood supply in fetuses with PA-VSD, as has already been reported in postnatal case series of PA-VSD[16]. In our case series, 2D echocardiography assessed correctly the anatomy of the central pulmonary arteries in only 8/12 (66.6%) patients and detected the source of the pulmonary blood supply in 75% of cases (Table 1). Both cases with non-confluent and hypoplastic pulmonary arteries were not assessed reliably.

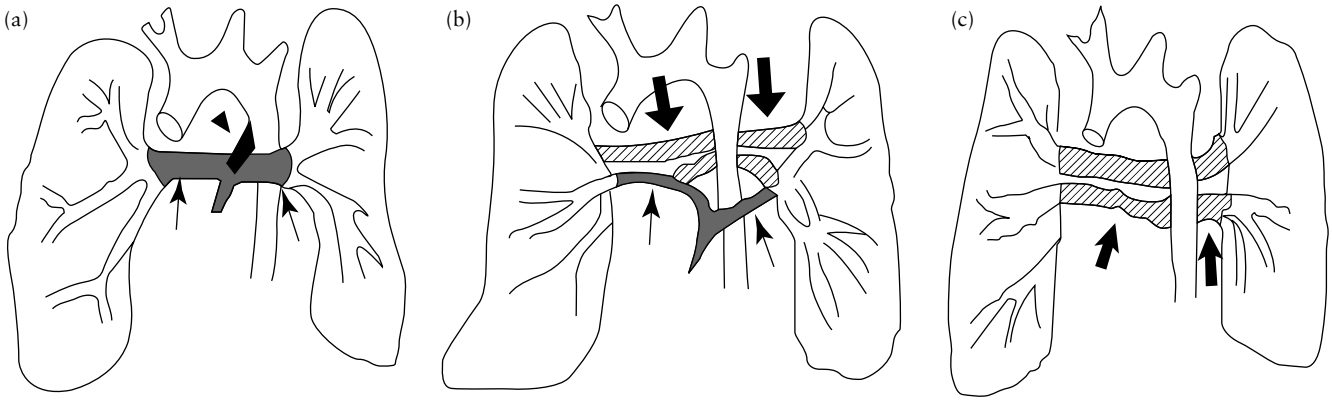

Figure 4 Schematic representation of the three main patterns of pulmonary arterial supply. (a) The left and right pulmonary arteries (arrows and gray shading) are confluent and are supplied by the ductus arteriosus (arrowhead and black). (b) The central pulmonary arteries (thin arrows and gray shading) are confluent and coexist with major aortopulmonary collateral arteries (MAPCA) (thick arrows and hatching). (c) There is complete absence of the central pulmonary arteries, the lung being supplied directly by multiple MAPCA (arrows and hatching).

Our study also found that B-flow imaging with STIC was able to visualize the pulmonary arteries and the source of the pulmonary blood supply in all five cases of PA-VSD examined; in fact, two of these cases (Cases 10 and 12) were overlooked by 2D echocardiography, one of them even escaping detection at postnatal echocardiography (Case 10) (Figure 3).

Reports have shown that 3D ultrasound can provide additional diagnostic information for the assessment of some facial and skeletal anomalies[27,28]. These rendered images may be especially helpful for assisting operators who counsel parents about the nature, prognosis and postnatal management of such malformations. Recently, it has been suggested that the use of 4D echocardiography with STIC and the 3D/4D 'inversion mode' rendering algorithm for the fetal heart and its vascular connections can provide information that may improve the prenatal visualization of some cardiac defects[21,29–31].

In conclusion, the findings presented here, although limited to a small sample size, support the superior ability of B-flow imaging and STIC, compared with 2D ultrasound, to visualize correctly very small vessels and pulmonary blood flow in fetuses with PA-VSD. 4D ultrasound may be used in the future to improve and help to detail the diagnosis of other fetal cardiac defects. This holds true in spite of the improvement in ultrasound equipment and operator experience over the years, since a comparison between the former period (1994–2003) and our most recent experience (2004–2005) failed to reveal a significant difference in the accuracy of the assessment of the anatomy of the pulmonary arteries and the sources of pulmonary blood flow in fetuses with PA-VSD by conventional 2D ultrasound.

REFERENCES

1. Haworth SG, Macartney FJ. Growth and development of pulmonary circulation in pulmonary atresia with ventricular septal defect and major aortopulmonary collateral arteries. *Br Heart J* 1980; **44**: 14–24.
2. Leonard H, Derrick G, O'Sullivan J, Wren C. Natural and unnatural history of pulmonary atresia. *Heart* 2000; **84**: 499–503.
3. Baker EJ. Tetralogy of Fallot with pulmonary atresia. In *Pediatric Cardiology*, Anderson RH, Macartney FJ, Shinebourne EA, Tynan M (eds). Churchill Livingstone: Edinburgh, UK, 2001; 1251–1279.
4. Hornberger LK. Tetralogy of Fallot. In *Textbook of Fetal Cardiology*, Allan L, Hornberger L, Sharland G (eds). Greenwich Medical Media: London, UK, 2000; 248–260.
5. Liao PK, Edwards WD, Julsrud PR, Puga FJ, Danielson GK, Feldt RH. Pulmonary blood supply in patients with pulmonary atresia and ventricular septal defect. *J Am Coll Cardiol* 1985; **6**: 1343–1350.
6. Chessa M, Butera G, Bonhoeffer P, Iserin L, Kachaner J, Lyonnet S, Munnich A, Sidi D, Bonnet D. Relation of genotype 22q11 deletion to phenotype of pulmonary vessels in tetralogy of Fallot and pulmonary atresia–ventricular septal defect. *Heart* 1998; **79**: 186–190.
7. Mahle WT, Crisalli J, Coleman K, Campbell RM, Tam VK, Vincent RN, Kanter KR. Deletion of chromosome 22q11.2 and outcome in patients with pulmonary atresia and ventricular septal defect. *Ann Thorac Surg* 2003; **76**: 567–571.
8. Boudjemline Y, Fermont L, Le Bidois J, Lyonnet S, Sidi D, Bonnet D. Prevalence of 22q11 deletion in fetuses with conotruncal cardiac defects: a 6-year prospective study. *J Pediatr* 2001; **138**: 520–524.
9. Chaoui R, Kalache KD, Heling KS, Tennsted C, Bommer C, Korner H. Absent or hypoplastic thymus on ultrasound: a marker for deletion 22q11.2 in fetal cardiac defects. *Ultrasound Obstet Gynecol* 2002; **20**: 546–552.
10. Volpe P, Marasini M, Caruso G, Marzullo A, Buonadonna AL, Arciprete P, Di Paolo S, Volpe G, Gentile M. 22q11 deletions in fetuses with malformations of the outflow tracts or interruption of the aortic arch: impact of additional ultrasound signs. *Prenat Diagn* 2003; **23**: 752–757.
11. Reddy VM, Liddicoat JR, Hanley FL. Midline one-stage complete unifocalization and repair of pulmonary atresia with ventricular septal defect and major aortopulmonary collaterals. *J Thorac Cardiovasc Surg* 1995; **109**: 832–844.
12. Bull K, Somerville J, Ty E, Spiegelhalter D. Presentation and attrition in pulmonary atresia. *J Am Coll Cardiol* 1995; **25**: 491–499.
13. Allan LD, Sharland GK, Milburn A, Lockhart SM, Groves AM, Anderson RH, Cook AC, Fagg NL. Prospective diagnosis of 1006 consecutive cases of congenital heart disease in the fetus. *J Am Coll Cardiol* 1994; **23**: 1452–1458.
14. Paladini D, Russo M, Teodoro A, Pacileo G, Capozzi G, Martinelli P, Nappi C, Calabro R. Prenatal diagnosis of congenital heart disease in the Naples area during the years 1994–99; the experience of a joint fetal-pediatric cardiology unit. *Prenat Diagn* 2002; **22**: 545–552.
15. Acherman RJ, Smallhorn JF, Freedom RM. Echocardiographic assessment of pulmonary blood supply in patients with pulmonary atresia and ventricular septal defect. *J Am Coll Cardiol* 1996; **28**: 1308–1313.
16. Smyllie JH, Sutherland GR, Keeton BR. The value of Doppler color flow mapping in determining pulmonary blood supply in infants with pulmonary atresia with ventricular septal defect *J Am Coll Cardiol* 1989; **14**: 1759–1765.
17. Deng J, Rodeck CH. New fetal cardiac imaging techniques. *Prenat Diagn* 2004; **24**: 1092–1103.
18. Pooh RK. New application of B-flow sonoangiography in perinatology. *Ultrasound Obstet Gynecol* 2000; **15**: 163.
19. Deane C. Extended field of view and B-flow ultrasound: fashion or future? *Ultrasound Obstet Gynecol* 2000; **15**: 96–97.
20. Pooh RK, Korai A. B-flow and B-flow spatio-temporal image correlation in visualizing fetal cardiac blood flow. *Croat Med J* 2005; **46**: 808–811.
21. Gonçalves LF, Espinoza J, Lee W, Nien JK, Hong JS, Santolaya-Forgas J, Mazor M, Romero R. A new approach to fetal echocardiography: digital casts of the fetal cardiac chambers and great vessels for detection of congenital heart disease. *J Ultrasound Med* 2005; **24**: 415–424.
22. Paladini D, Chita SK, Allan LD. Prenatal measurement of cardiothoracic ratio in evaluation of heart disease. *Arch Dis Child* 1990; **65**: 20–23.
23. Tan J, Silverman NH, Hoffman JI, Villegas M, Schmidt KG. Cardiac dimensions by cross-sectional echocardiography in the normal human fetus from 18 weeks to term. *Am J Cardiol* 1992; **70**: 1459–1467.
24. Tometzki AJ, Suda K, Kohl T, Kovalchin JP, Silverman NH. Accuracy of prenatal echocardiographic diagnosis and prognosis of fetuses with conotruncal anomalies. *J Am Coll Cardiol* 1999; **33**: 1696–1701.
25. Volpe P, Paladini D, Marasini M, Buonadonna AL, Russo MG, Caruso G, Marzullo A, Vassallo M, Martinelli P, Gentile M. Common arterial trunk in the fetus: characteristics, associations, and outcome in a multicentre series of 23 cases. *Heart* 2003; **89**: 1437–1441.
26. Shimazaki Y, Maehara T, Blackstone EH, Kirklin JW, Bargeron LM Jr. The structure of the pulmonary circulation in tetralogy of Fallot with pulmonary atresia. *J Thorac Cardiovasc Surg* 1988; **95**: 1048–1058.

27. Merz E, Weber G, Bahlmann F, Miric-Tesanic D. Application of transvaginal and abdominal 3D ultrasound for the detection or exclusion of malformations of the fetal face. *Ultrasound Obstet Gynecol* 1997; **9**: 237–243.
28. Krakow D, Williams J 3rd, Poehl M, Rimoin DL, Platt LD. Use of three-dimensional ultrasound imaging in the diagnosis of prenatal-onset skeletal dysplasias. *Ultrasound Obstet Gynecol* 2003; **21**: 467–472.
29. DeVore GR, Falkensammer P, Slansky MS, Platt LD. Spatio-temporal image correlation (STIC): new technology for evaluation of fetal heart. *Ultrasound Obstet Gynecol* 2003; **22**: 380–387.
30. Chaoui R, Hoffman J, Heling KS. Three-dimensional (3D) and 4D color Doppler fetal echocardiography using spatio-temporal image correlation (STIC). *Ultrasound Obstet Gynecol* 2004; **23**: 535–545.
31. Espinoza J, Gonçalves LF, Lee W, Mazor M, Romero R. A novel method to improve prenatal diagnosis of abnormal systemic venous connections using three and four-dimensional ultrasonography and "inversion mode". *Ultrasound Obstet Gynecol* 2005; **25**: 428–434.

