



Dynamics of the Pulmonary Venous Flow in the Fetus and Its Association With Vascular Diameter

Paulo Zielinsky, Antônio Piccoli, Jr, Eduardo Gus, João Luiz Manica, Fabíola Satler, Luiz Henrique Nicoloso, Stelamaris Luchese, Silvana Marcantonio, Marlui Scheid and Domingos Hatém

Circulation. 2003;108:2377-2380; originally published online October 13, 2003; doi: 10.1161/01.CIR.0000093195.73667.52 Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231 Copyright © 2003 American Heart Association, Inc. All rights reserved. Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at: http://circ.ahajournals.org/content/108/19/2377

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at: http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Circulation* is online at: http://circ.ahajournals.org//subscriptions/

Dynamics of the Pulmonary Venous Flow in the Fetus and Its Association With Vascular Diameter

Paulo Zielinsky, MD, PhD; Antônio Piccoli, Jr, MD; Eduardo Gus, MD; João Luiz Manica, MD; Fabíola Satler, MD; Luiz Henrique Nicoloso, MD, MSc; Stelamaris Luchese, MD, MSc; Silvana Marcantonio, MD, MSc; Marlui Scheid, MD; Domingos Hatém, MD, MSc

- *Background*—The usual positioning of the Doppler sample volume to assess fetal pulmonary vein flow is in the distal portion of the vein, where the vessel diameter is maximal. This study was performed to test the association of the pulmonary vein pulsatility index (PVPI) with the vessel diameter.
- *Methods and Results*—Twenty-three normal fetuses (mean gestational age, 28.6 ± 5.3 weeks) were studied by Doppler echocardiography. Pulmonary right upper vein flow was assessed adjacent to the venoatrial junction ("distal" position) and in the middle of the vein ("proximal" position). The vessel diameter was measured by 2D echocardiography with power Doppler, and the PVPI was obtained by the ratio (maximal velocity [systolic or diastolic peak]—minimal velocity [presystolic peak])/mean velocity. The statistical analysis used *t* test and exponential correlation studies. Mean distal diameter was 0.33 ± 0.10 cm (0.11 to 0.57 cm), and mean proximal diameter was 2.016 ± 0.08 cm (0.11 to 0.25 cm) (*P*<0.0001). Mean distal PVPI was 0.84 ± 0.21 (0.59 to 1.38), and mean proximal PVPI was 2.09 ± 0.59 (1.23 to 3.11) (*P*<0.0001). Exponential inverse correlation between pulmonary vein diameter and pulsatility index was highly significant (*P*<0.0001), with a determination coefficient of 0.439.
- *Conclusions*—In the normal fetus, the pulmonary venous flow pulsatility decreases from the lung to the heart, and this parameter is inversely correlated to the diameter of the pulmonary vein, which increases from its proximal to its distal portion. This study emphasizes the importance of the correct positioning of the Doppler sample volume, adjacent to the venoatrial junction, to assess pulmonary venous flow dynamics. (*Circulation.* 2003;108:2377-2380.)

Key Words: fetus ■ echocardiography ■ blood flow ■ physiology ■ vessels

Fetal Doppler echocardiography is an expanding field, and functional studies are now an essential part of the routine examination.

The paramount importance of the events taking place in the left atrium, such as flow through the foramen ovale, coming from the ductus venosus, mitral flow patterns, and flow from the pulmonary veins, are directly related to left atrial pressure and volume and to left ventricular relaxation and compliance. Analysis of the pulmonary vein flow has been used along with other parameters in the assessment of fetal diastolic function.^{1,2} The pulmonary vein pulsatility index (PVPI) reflects the relative impedance to the forward flow and is believed to be better comparable than absolute values of individual waveforms and independent of the insonation angle.³ The standard position of the Doppler sample volume to obtain the pulmonary vein flow is in the distal portion of the vein, adjacent to the venoatrial junction, where the vessel diameter is maximal. Morphometric studies of the pulmonary venous vasculature confirm that the pulmonary veins show a tapering pattern from the left atrium to the hylum,4,5 and mathematical models show that the flow wave is altered by the change in the cross-sectional area of the vessel.^{6–10} It seemed logical to suppose that if the Doppler sampling were performed more proximally, in a region where the pulmonary vein size was smaller, the results could be different, possibly expressing an increased impedance to the forward flow where the vessel was narrower.

Thus, this study was performed to test the hypothesis that the PVPI should be lower in the venoatrial junction than at a more proximal site and that this behavior should be correlated to the progressive decrease in the vessel diameter from the left atrium toward the lung.

Methods

Twenty-three normal fetuses, with a mean gestational age of 28.6 ± 5.3 weeks (20 to 36 weeks) were studied by cross-sectional and Doppler echocardiography. Any maternal or fetal abnormalities excluded the patient from the study. Commercially available equipment with 2D, M-mode, pulsed, and continuous Doppler; color flow mapping; and power angio-Doppler capabilities was used.

Considering the established reproducibility of transthoracic pulmonary venous Doppler flow indices,¹¹ intraobserver and interobserver variability was not calculated.

Circulation is available at http://www.circulationaha.org

DOI: 10.1161/01.CIR.0000093195.73667.52

Received April 28, 2003; revision received July 11, 2003; accepted July 11, 2003.

From the Fetal Cardiology Unit, Institute of Cardiology of Rio Grande do Sul, Porto Alegre, Brazil.

Correspondence to Dr Paulo Zielinsky, Instituto de Cardiologia do Rio Grande do Sul, Unidade de Pesquisa, Av Princesa Isabel, 370, Santana, Porto Alegre Zip 90.620-001. E-mail pesquisa@cardnet.tche.br or zielinsky@cardiol.br

^{© 2003} American Heart Association, Inc.



Figure 1. Right upper pulmonary (PULM) vein imaging in a 33-week fetus by 2D echocardiography enhanced by power Doppler. Notice progressive increase of vessel diameter toward left atrium (LA).

Pulmonary venous flow was assessed in the upper right vein at 2 different sites: adjacent to the opening to the left atrium ("distal" position) and in the middle of the vein ("proximal" position), below the level of the middle lobe vein.¹² The vessel diameter was measured at the 2 sites by 2D echocardiography enhanced with power Doppler (Figure 1). PVPI was obtained by the pulsed Doppler ratio, as follows: (maximal velocity [systolic or diastolic peak]–minimal velocity [presystolic peak])/mean velocity, electronically calculated by the equipment after manual tracing of the pulmonary waveforms during the entire cardiac cycle (Figure 2). The mean of 5 measurements was considered, in the absence of fetal breathing movements.

Informed consent was obtained in every case.

Statistical analysis used t test and exponential correlation studies, with a confidence limit of 99%.

Results

Mean distal internal diameter was 0.33 ± 0.10 cm (0.11 to 0.57 cm), with a median of 0.32 cm, and mean proximal



Figure 2. Doppler tracing of a typical distal pulmonary vein flow. Velocities were electronically calculated after manual tracing of waveforms. Presystolic velocity is 0.09 m/s, and calculated pulsatility index is 1.21.

diameter was 0.16 ± 0.08 cm (0.11 to 0.25 cm), with a median of 0.16 cm (*P*<0.0001) (Figure 3).

There was no statistical difference between mean systolic (S wave) and diastolic (D wave) peak velocities at the 2 sites (distal $S=0.20\pm0.09$ m/s [0.17 to 0.58 m/s], proximal $S=0.22\pm0.08$ m/s [0.14 to 0.52 m/s]; distal $D=0.21\pm0.09$ m/s [0.14 to 0.53 m/s], proximal $D=0.19\pm0.14$ m/s [0.10 to 0.53 m/s]).

Mean peak presystolic velocity (A wave) was significantly higher in the distal position (A= 0.12 ± 0.04 m/s [0.06 to 0.16 m/s]) than at the proximal site (A= -0.12 ± 0.07 m/s [-0.13 to 0.09 m/s]) (P=0.002).



Figure 3. Diagram showing median distal and proximal pulmonary vein (PV) diameters. Horizontal bars above and below median boxes represent maximal and minimal values of PV diameter.



Figure 4. Diagram showing median distal and proximal PVPIs. Horizontal bars above and below median boxes represent maximal and minimal values of PVPI.

Mean distal PVPI was 0.84 ± 0.21 (0.59 to 1.38), with a median of 0.77, and mean proximal PVPI was 2.09 ± 0.59 (1.23 to 3.11), with a median of 2.22 (*P*<0.0001) (Figure 4).

Exponential inverse correlation between pulmonary vein diameter and pulsatility index was highly significant (P<0.0001), with a determination coefficient of 0.439 (Figure 5).

Discussion

Studies on human embryonic and fetal lungs demonstrate that the pulmonary arteries form by vasculogenesis,¹³ but there is less information on the early development of the pulmonary veins. Studies on maturation of pulmonary venous smooth muscle suggest that a developmentally regulated remodeling of the vein walls may reduce resistance to blood flow in fetal life.¹⁴ It has also been shown that the development of the airways and pulmonary veins occurs at different times and that the branching patterns of these structures are not interdependent.^{15–17} The common pulmonary vein develops within the sinus venosus segment¹⁸ and is later incorporated into the morphological left atrium.¹⁹ Morphometric studies in ani-



Figure 5. Diagram depicting inverse correlation between PVPI and vessel diameter.

mals⁴ and in humans⁵ demonstrate that the branching patterns of the pulmonary veins show many orders of tapering, from the left atrium, where the diameter of the vessel (and its cross-sectional area) is maximal, toward the pulmonary bed, where it is minimum.

An experimental hemodynamic study showed that the pulmonary vein pressure varied depending on the recording site, resembling pulmonary artery pressure closer to the pulmonary capillary bed and left atrial pressure closer to the venoatrial junction.²⁰ The same rationale applies when the flow velocities from the lung to the heart are considered, with the pulmonary vein diameter at the different sites probably being the main determinant, as is demonstrated in the present study. Other factors involved have been evaluated, such as left atrium relaxation and compliance and left ventricular function.^{21–27} Pulmonary vein relaxation, mediated by C-type natriuretic peptide, is uniform and thus does not allow segmental variations.²⁸

The effects of vessel tapering in the pulmonary circulation have been studied by nonlinear models,^{6,10} and the role of the vessel cross-sectional area in the flow wave dynamics has also been assessed.⁷ A theoretical model designed to evaluate the wave transmission in a stenotic tube suggests that nonsevere stenoses may cause significant wave reflections,⁸ which is consistent with the idea that the flow impedance is related to the diameter of the tube.

Because Doppler analysis of the pulmonary venous waveforms is widely used in clinical practice,^{1-3,29–35} it is imperative to have the sample volume correctly positioned in the distal portion of the pulmonary vein, near the venoatrial junction, to achieve reliable results, because this fetal study showed that the presystolic velocity decreases and the pulsatility index increases when a more proximal site is sampled.

It has been demonstrated that, in the normal fetus, the pulsatility of the pulmonary vein decreases along the way from the lung to the heart and that this parameter is inversely correlated to the cross-sectional diameter of the pulmonary vein, which increases from the proximal to the distal portion of the vessel.

References

- Hong YM, Choi JY. Pulmonary venous flow from fetal to neonatal period. *Early Hum Dev*. 2000;57:95–103.
- Crowe DA, Allan LD. Patterns of pulmonary venous flow in the fetus with disease of the left heart. *Cardiol Young*. 2001;11:369–374.
- Lenz F, Chaoui R. Reference ranges for Doppler-assessed pulmonary venous blood flow velocities and pulsatility indices in normal human fetuses. *Prenat Diagn.* 2002;22:786–791.
- Gan RZ, Tian Y, Yen RT, et al. Morphometry of the dog pulmonary venous tree. J Appl Physiol. 1993;75:432–440.
- Huang W, Yen RT, McLaurine M, et al. Morphometry of the human pulmonary vasculature. J Appl Physiol. 1996;81:2123–2133.
- Lucas CL. Fluid mechanics of the pulmonary circulation. Crit Rev Biomed Eng. 1984;10:317–393.
- Demiray H. Waves in initially stressed fluid-filled thick tubes. J Biomech. 1997;30:273–276.
- Stergiopulos N, Spiridon M, Pythoud F, et al. On the wave transmission and reflection properties of stenoses. J Biomech. 1996;29:31–38.
- Huang W, Tian Y, Gao J, et al. Comparison of theory and experiment in pulsatile flow in cat lung. *Ann Biomed Eng.* 1998;26:812–820.
- Segers P, Verdonck P. Role of tapering in aortic wave reflection: hydraulic and mathematical model study. J Biomech. 2000;33:299–306.

- Hole T, Urheim S, Skjaerpe T. Intra- and inter-observer reproducibility of transthoracic pulmonary venous Doppler flow indices after acute myocardial infarction. *Eur J Echocardiogr.* 2002;3:32–38.
- Yazar F, Ozdogmus O, Tuccar E, et al. Drainage patterns of middle lobe vein of right lung: an anatomical study. *Eur J Cardiothorac Surg.* 2002; 22:717–720.
- Hall SM, Hislop AA, Pierce CM, et al. Prenatal origins of human intrapulmonary arteries: formation and smooth muscle maturation. *Am J Respir Cell Mol Biol.* 2000;23:194–203.
- 14. Fasouliotis SJ, Achiron R, Kivilevitch Z, et al. The human fetal venous system: normal embryologic, anatomic, and physiologic characteristics and developmental abnormalities. *J Ultrasound Med.* 2002;21: 1145–1158.
- DeMello DE, Reid LM. Embryonic and early fetal development of human lung vasculature and its functional implications. *Pediatr Dev Pathol*. 2000;3:439–449.
- Hislop AA. Airway and blood vessel interaction during lung development. J Anat. 2002;201:325–334.
- Hall SM, Hislop AA, Haworth SG. Origin, differentiation, and maturation of human pulmonary veins. Am J Respir Cell Mol Biol. 2002;26:333–340.
- Blom NA, Gittenberger-de-Groot AC, Jongeneel TH, et al. Normal development of the pulmonary veins in human embryos and formulation of a morphogenetic concept for sinus venosus defects. *Am J Cardiol.* 2001; 87:305–309.
- Webb S, Kanani M, Anderson RH, et al. Development of the human pulmonary vein and its incorporation into the morphologically left atrium. *Cardiol Young*. 2001;11:632–642.
- Appleton CP. Hemodynamic determinants of Doppler pulmonary venous flow velocity components: new insights from studies in lightly sedated normal dogs. J Am Coll Cardiol. 1997;30:1562–1574.
- Barbier P, Solomon S, Schiller NB, et al. Determinants of forward pulmonary vein flow: an open pericardium pig model. *J Am Coll Cardiol.* 2000;35:1947–1959.
- 22. Talbert DG, Johnson P. The pulmonary vein Doppler flow velocity waveform: feature analysis by comparison of in vivo pressures and flows with those in a computerized fetal physiological model. *Ultrasound Obstet Gynecol.* 2000;16:457–467.

- Smiseth OA, Thompson CR, Lohavanichbutr K, et al. The pulmonary venous systolic flow pulse: its origin and relationship to left atrial pressure. J Am Coll Cardiol. 1999;34:802–809.
- Rajagopalan B, Friend JA, Stallard T, et al. Blood flow in pulmonary veins, I: studies in dog and man. *Cardiovasc Res.* 1979;13:667–676.
- Rajagopalan B, Friend JA, Stallard T, et al. Blood flow in pulmonary veins, II: the influence of events transmitted from the right and left sides of the heart. *Cardiovasc Res.* 1979;13:677–683.
- Rajagopalan B, Bertram CD, Stallard T, et al. Blood flow in pulmonary veins, III: simultaneous measurements of their dimensions, intravascular pressure and flow. *Cardiovasc Res.* 1979;13:684–692.
- Hellevik LR, Segers P, Stergiopulos N, et al. Mechanism of pulmonary venous pressure and flow waves. *Heart Vessels*. 1999;14:67–71.
- Lakshminrusimha S, D'Angelis CAD, Russell JA, et al. C-type natriuretic peptide system in fetal ovine pulmonary vasculature. *Am J Physiol Lung Cell Mol Physiol*. 2001;281:L361–L368.
- Rossi A, Loredana L, Cicoira M, et al. Additional value of pulmonary vein parameters in defining pseudonormalization of mitral inflow pattern. *Echocardiography*. 2001;18:673–679.
- Graziano JN, Heidelberger KP, Ensing GJ, et al. The influence of a restrictive atrial septal defect on pulmonary vascular morphology in patients with hypoplastic left heart syndrome. *Pediatr Cardiol.* 2002;23: 146–151.
- 31. Lenz F, Machlitt A, Hartung J, et al. Fetal pulmonary venous flow pattern is determined by left atrial pressure: report of two cases of left heart hypoplasia, one with patent and the other with closed interatrial communication. Ultrasound Obstet Gynecol. 2002;19:392–395.
- Yalcin F, El-Amrousy M, Muderrisoglu H, et al. Pulmonary venous flows reflect changes in left atrial hemodynamics during mitral balloon valvotomy. *Angiology*. 2002;53:323–327.
- Palazzuoli A, Puccetti L, Pastorelli M, et al. Transmitral and pulmonary venous flow study in elite male runners and young adults. *Int J Cardiol.* 2002;84:47–51.
- 34. Yang H, Jones M, Shiota T, et al. Pulmonary venous flow determinants of left atrial pressure under different loading conditions in a chronic animal model with mitral regurgitation. J Am Soc Echocardiogr. 2002:15(10 pt 2):1181–1218.
- Ito T, Harada K, Takada G. Changes in pulmonary venous flow patterns in patients with ventricular septal defect. *Pediatr Cardiol.* 2002;23: 491–495.