

THE DEVELOPMENT OF THE PULMONARY TRUNK AND THE PULMONARY ARTERIES IN THE HUMAN FETUS

Dariusz Nowak¹, Hanna Kozłowska^{2,3}, Anna Żurada³, Jerzy Gielecki³

¹ Department of Histology and Embryology, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Poland

² NeuroRepair Department, The Mossakowski Medical Research Center, Polish Academy of Sciences, Warsaw, Poland

³ Department of Anatomy, Faculty of Medical Sciences, University of Warmia and Mazury in Olsztyn, Poland

ABSTRACT

Introduction. Up to date studies dealing with embryogenesis of the pulmonary trunk and arteries seldom analyze the anatomical variations between sexes and proportions of the pulmonary arteries dimensions. A large number of investigated subjects in our study enabled a detailed description of the growth of the pulmonary trunk and pulmonary arteries. Other studies involved fewer subjects.

Aim. We aimed at investigating the development of the pulmonary trunk and its branches, i.e., the left and the right pulmonary arteries, during a period between the 4th and 8th months of fetal life.

Materials and methods. We investigated 223 human fetuses, including 108 males and 115 females, aged between 4 and 8 months of prenatal life. All fetuses had been conserved for a minimum period of 3 months in a 9% formaldehyde solution. All fetuses of a normal karyotype were obtained from spontaneous abortions and none of them revealed any external signs of malformations. We measured the diameters of the initial part of the pulmonary trunk and of the two main arteries: right and left pulmonary arteries. We determined the mean value of each assessed parameter for every age group, the rate of growth of particular vessels, the variations in these parameters with relation to sex, and the ratio between the left and the right pulmonary artery dimensions. For statistical analysis ANOVA, regression analysis, and Tukey's HSD post hoc test were used.

Corresponding address: Dariusz Nowak, Katedra i Zakład Histologii i Embriologii, Collegium Medicum, ul. Karłowicza 24, 85-092 Bydgoszcz, Poland; phone: +48 607 82 80 05, fax: +48 523 73 60 97, e-mail: dareknowak15@wp.pl

Received 24.11.2010, accepted 3.01.2011

Results, Discussion and Conclusions. The growth of the diameters of pulmonary vessels (pulmonary trunk, left and right pulmonary arteries) is linear in time. The vessel dimensions do not differ with regard to sex. Only in the 5th month was the pulmonary trunk statistically significantly wider in female fetuses. The left pulmonary artery is smaller than the right one.

Key words: pulmonary artery, prenatal development, human fetus

INTRODUCTION

Autopsy serves as an important and relevant source of information concerning the development of the human circulatory system in prenatal life. Other methods, such as radiographic imaging, cannot be widely employed being deleterious to the growing organism. Echocardiography is a useful, complimentary method as it employs harmless radiation. It is not free from limitations however; not all cardiac structures and large vessels, such as the pulmonary trunk and its divisions, can be visualized in detail [3]. The importance of investigating the embryogenesis of pulmonary arterial vessels arises from discrepancies in cardiovascular anatomy between fetal and postnatal life. The assessment of diameters of these vessels is valuable in diagnosing and monitoring congenital heart defects. Frequently, heart defects show up as, or co-occur with, abnormalities of the major arteries – including the pulmonary trunk and its branches [2, 3, 5, 7, 8, 12, 14, 17, 21, 28, 34, 36, 38].

AIM

We aimed at investigating the development of the pulmonary trunk and its branches, i.e., the left and the right pulmonary arteries, during that period between the 4th and 8th months of fetal life. We also investigated sex related differences concerning the diameters of these vessels. Also, we assessed the relationship between the dimensions of the left and the right pulmonary arteries.

MATERIALS AND METHODS

Research material consisted of 223 human fetuses, including 108 males and 115 females, aged between 4–8 months of prenatal life. The entire material for this project was obtained from the Department of Histology and Embryology of the Collegium Medicum of Nicolaus Copernicus University in Bydgoszcz, Poland. The fetuses had been conserved for a minimum period of 3 months in a 9% formaldehyde solution. All fetuses of a normal karyotype had been aborted spontaneously. None of them demonstrated any external signs of malformations or developmental abnormalities. The morphological age of each fetus was determined according to the crown-rump length (vertex-tuberales) using a polynomial initially proposed by Iffy et al. [19]. All

specimens were categorized into monthly subgroups according to the determined morphological age. Different numbers of fetuses were allocated to particular age groups.

The vessel beds were filled with latex LBS 3060, without distorting the dimensions of the vessels, at an amount of approximately 15–30 mL, through a catheter, which was inserted by dorsal access into the thoracic aorta. During specimen preparation we used binocular magnifying glasses (MBS-9, Russia, magnification $0.6-7 \times 14$). The measurements were taken using digital calipers (INCO, Poland, resolution 0.01mm) with an accuracy range of 0.01 mm. We measured the diameter of the initial segment of the pulmonary trunk (PT) and the diameters of the right (RPA) and the left (LPA) pulmonary arteries – also in their initial segments (Fig. 1, 2). All measurements were taken by two independent investigators. Each investigator took the measurements twice. For further analyses the arithmetical means of the obtained values were used.

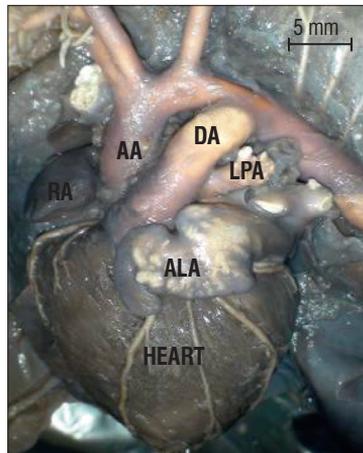


Fig. 1. Heart and the great arteries of a 28-weeks old female fetus, anterior surface. Comments: AA – ascending aorta, PT – pulmonary trunk, LPA – left pulmonary artery, DA – ductus arteriosus, ARA – auricle right atrium, ALA – auricle left atrium

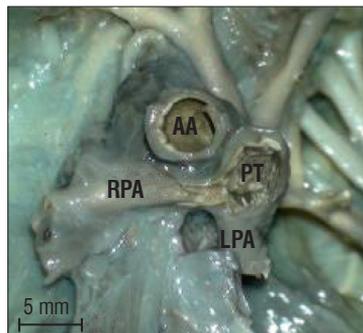


Fig. 2. The great arteries of a 24-weeks old male fetus, view from the diaphragmatic surface, the heart was removed. Comments: AA – ascending aorta, PT – pulmonary trunk, LPA – left pulmonary artery, DA – ductus arteriosus, ARA – auricle right atrium, ALA – auricle left atrium

Statistica 8.0 software (StatSoft Polska) was used for statistical analysis of the obtained data. We calculated mean values and standard deviations for each age group with respect to sex. The results obtained were analyzed by the one-way ANOVA test for unpaired data (age) and two-way ANOVA test for unpaired data (age and sex), and Tukey's HSD post hoc test for non-equal populations. The differences between pulmonary artery dimensions were analyzed using a two-way (side of the body and age) analysis of variances (ANOVA) for dependent variables and Tukey's HSD post hoc test for non-equal populations. Statistical significance was defined as $p \leq 0.05$.

RESULTS

The diameter of the pulmonary trunk increases according to the linear regression curve $y = -86.8853 + 0.8744x$. Initially, in the 4th month, the diameter of the pulmonary trunk was 1.51 ± 0.24 mm, and it grew to 4.85 ± 0.31 mm by the 8th month (Tab. 1). The pulmonary trunk diameter correlation coefficient for age was $r = 0.9364$, and it was highly statistically significant ($p < 0.001$) (Fig. 3). We found no significant sex differences in the pulmonary trunk diameter within each group ($p = 0.2945$). Only in the 5th month was that diameter larger in females ($p = 0.0084$) (Tab. 1). The diameter of the right pulmonary artery also increases according to the linear regression curve $y = -48.9848 + 0.4925x$. The correlation coefficient for age was $r = 0.8873$, with a high level of significance $p < 0.001$ (Fig. 4). In the 4th month the right pulmonary artery diameter was 0.69 ± 0.18 mm, and it grew to 2.74 ± 0.31 mm by the 8th month (Tab. 2). The diameter of the right pulmonary artery within the entire group was 1.59 ± 0.51 mm. There were no sex related differences with regard to that vessel's diameter ($p > 0.05$), neither in the whole study group ($p = 0.2603$) nor within particular age groups (Tab. 2).

Tab. 1. Mean pulmonary trunk diameter in particular monthly age groups shown for the entire group and with regard to sex

Age [month]	N			X±SD [mm]			P value
	total	male	female	total	male	female	
4	18	8	10	1.51±0.24	1.44±0.28	1.57±0.2	0.3162
5	70	32	38	2.34±0.24*	2.22±0.22*	2.44±0.22*	0.0084
6	105	50	55	3.26±0.32*	3.27±0.32*	3.24±0.33*	0.6091
7	18	12	6	3.95±0.39*	3.95±0.39*	3.94±0.45*	0.9957
8	12	6	6	4.85±0.31*	4.86±0.24*	4.83±0.39*	0.8639
Total	223	108	115	2.93±0.86	2.99±0.88	2.87±0.84	0.2945

Comments: * - indicates statistically significant difference of the marked subgroup when compared to the immediately younger subgroup ($p < 0.05$), N - number, X - parameter value, SD - standard deviation, P value - the differences between mean values in the female and male fetuses in particular age groups ($p < 0.05$).

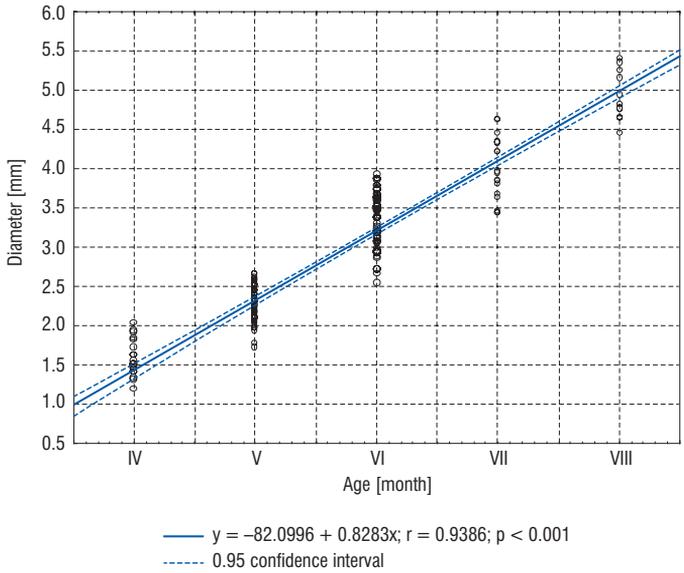


Fig. 3. Regression curve for the pulmonary trunk diameter versus fetal age (x)

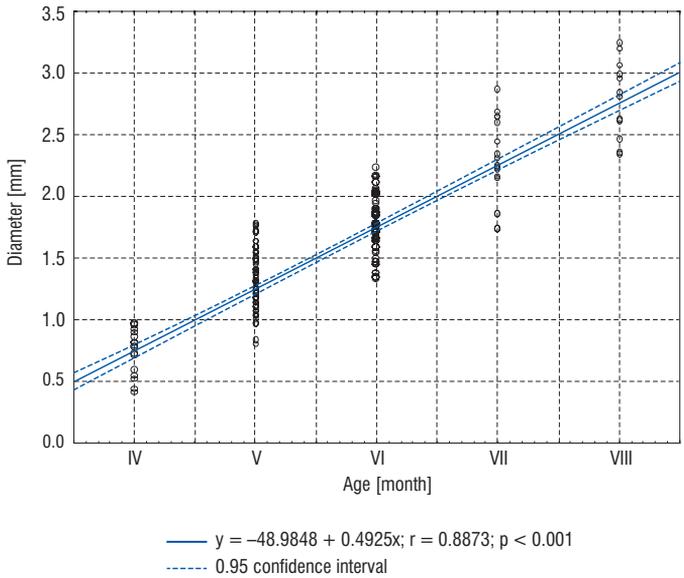


Fig. 4. Regression curve for the right pulmonary artery diameter versus fetal age (x)

Tab. 2. Mean right pulmonary artery diameter in particular monthly age groups shown for the entire group and with regard to sex

Age [month]	N			X±SD [mm]			P value
	total	male	female	total	male	female	
4	18	8	10	0.69±0.18	0.70±0.18	0.69±0.19	0.9540
5	70	32	38	1.27±0.23*	1.26±0.24*	1.28±0.22*	0.7361
6	105	50	55	1.74±0.22*	1.75±0.22*	1.73±0.21*	0.6508
7	18	12	6	2.19±0.36*	2.23±0.38*	2.11±0.33*	0.5279
8	12	6	6	2.74±0.31*	2.80±0.33*	2.69±0.32*	0.5717
Total	223	108	115	1.59±0.51	1.64±0.54	1.56±0.48	0.2603

Comments: * - indicates statistically significant difference of the marked subgroup when compared to the immediately younger subgroup ($p < 0.05$), N - number, X - parameter value, SD - standard deviation, P value - the differences between mean values in the female and male fetuses in particular age groups ($p < 0.05$).

The average diameter of the left pulmonary artery within the entire group was 1.33 ± 0.40 mm. It ranged from 0.78 ± 0.22 mm in the 4th month to 2.2 ± 0.18 mm by the 8th month of prenatal life (Tab. 3). The growth of the diameter of the left pulmonary artery was reflected in a linear regression curve $y = -35.0635 + 0.3544x$. The correlation coefficient was $r = 0.8128$, which was highly statistically significant ($p < 0.001$) (Fig. 5). There were no significant sex differences with regard to that parameter within the entire study group ($p = 0.2465$), nor within particular age groups ($p > 0.05$) (Tab. 3).

Tab. 3. Mean left pulmonary artery diameter in particular monthly age groups shown for the entire group and with regard to sex

Age [month]	N			X±SD [mm]			P value
	total	male	female	total	male	female	
4	18	10	8	0.78±0.22	0.86±0.17	0.72±0.25	0.2036
5	70	32	38	1.12±0.21*	1.12±0.20*	1.13±0.21*	0.7585
6	105	50	55	1.36±0.22*	1.36±0.25*	1.36±0.19*	0.9811
7	18	12	6	1.98±0.3*	2.03±0.32*	1.9±0.26*	0.4277
8	12	6	6	2.2±0.18*	2.14±0.19*	2.27±0.17*	0.2501
Total	223	108	115	1.33±0.40	1.37±0.42	1.31±0.39	0.2465

Comments: * - indicates statistically significant difference of the marked subgroup when compared to the immediately younger subgroup ($p < 0.05$), N - number, X - parameter value, SD - standard deviation, P value - the differences between mean values in the female and male fetuses in particular age groups ($p < 0.05$).

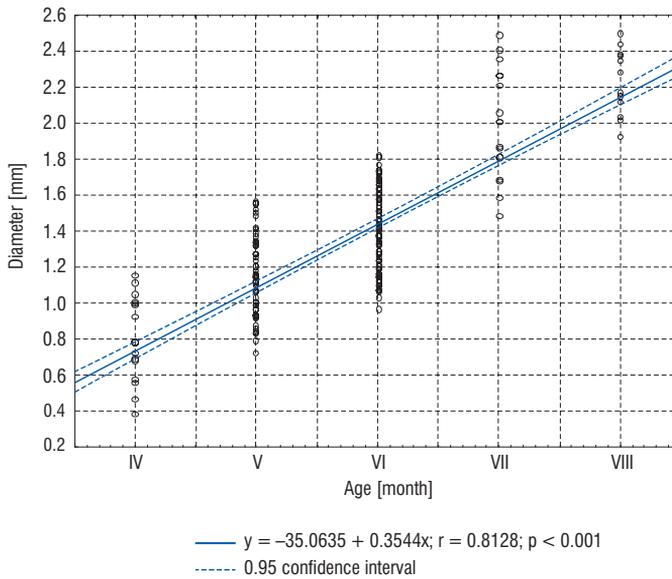


Fig. 4. Regression curve for the left pulmonary artery diameter versus fetal age (x)

The development of the pulmonary trunk and of the left and the right pulmonary arteries in consecutive months showed significant dimension changes when compared to preceding months. These differences were notable in the entire group between the 5th and the 6th, the 6th and the 5th, the 7th and the 6th, the 8th and the 7th months. As far as the sex of fetuses was concerned, these differences were marked between the 5th and the 4th, the 6th and the 5th, the 7th and the 6th, and the 8th and the 7th months, both in females and males (Tab. 1–3).

We found a significant difference between the dimensions of the two main pulmonary arteries ($p=0.0031$). The right pulmonary artery was consistently larger. The ratio of the two diameters calculated for the entire group was 1.21 ± 0.27 and it changed in time only slightly and insignificantly ($p\geq 0.05$) within a range from 1.08 to 1.25 (Tab. 4). Also, this ratio did not differ statistically significantly between sexes ($p>0.05$).

Tab. 4. The ratio of the right to left pulmonary artery diameters (x)

Age [months]	N	X	SD
4	18	1.08	0.09
5	70	1.16	0.26
6	105	1.21	0.27
7	18	1.12	0.21
8	12	1.25	0.15
Total	223	1.21	0.27

Comments: SD – standard deviation. There is no difference between consecutive age groups ($p>0.05$).

DISCUSSION

In this study we found that the pulmonary trunk and arteries growth rates have a linear pattern. Similar results were found in other studies where echocardiography [28, 38, 39] or autopsy [4, 6, 24] were used. Also, Szpinda et al. [31, 32] found that the growth of the pulmonary trunk was proportional to fetal age and followed a linear regression. This was found at the correlation coefficient for age $r=0.86$ ($p<0.001$). Alvarez et al. [4], who also described a linear growth pattern concerning the pulmonary trunk, pointed to a highly statistically significant correlation coefficient ($r=0.852$; $p<0.0001$). Hyett et al. [18] in their study concerning 61 fetuses aged between 3 and 5 months, plotted a linear regression curve showing the relationship between the diameter of the pulmonary trunk and age ($r=0.889$, $p<0.0001$). These autopsy findings confirm echocardiographic observations. Studies of Chaoui et al. [10] and Gembruch et al. [15] demonstrated a linear pattern of the pulmonary trunk growth. Also Achiron et al. [1] in their study concerning 139 fetuses, aged between 4 and 7 months, and Firpo et al. [13] in their study concerning 181 fetuses, aged between 4 and 9 months, proved that the diameter of the pulmonary trunk grew linearly in time. The correlation coefficient was very high in both studies: $r=0.94$ ($p<0.0001$) according to Achiron et al. [1], and $r=0.9081$ ($p<0.01$) according to Firpo et al. [13]. Similar findings were reported for the pulmonary arteries diameters. A linear growth rate of the fetal pulmonary arteries was confirmed both in anatomical [4, 18, 33, 37] and echocardiographic studies [13, 17]. We found the diameter of the right pulmonary artery to be consistently larger than the left one ($p<0.001$). This is in accordance with other authors' findings [6, 9, 11, 16, 20, 27, 30, 31, 33]. Only Tan et al. [35] in their study concerning fetuses aged between 6 and 9 months did not find any difference between the diameters of the two main pulmonary arteries ($p=0.254$).

The diameters of the pulmonary trunk, the left and the right pulmonary arteries that we found in our material are similar to data presented in available literature. Ursell et al. [37] discovered that the diameter of the pulmonary trunk was 1.1 mm before the 3rd month, 2.0 mm in the 4th month, 2.5 mm in the 5th month, and 3.5 mm following the 6th month of fetal life. Castillo et al. [9] in their material consisting of 103 fetuses, aged between 4 and 9 months, found that the pulmonary trunk diameter ranged from 2.1 mm to 4.2 mm. The diameter of the right pulmonary artery was 1.2–2.5 mm, and the left one 0.9–2.18 mm [9]. Szpinda [32] found the diameter of the pulmonary trunk in the 4th month to be 1.51 mm, and in consecutive months: the 5th – 2.44 mm, the 6th – 3.79 mm, the 7th – 4.16 mm, the 8th – 5.15 mm. Also according to Szpinda [33], the left pulmonary artery diameter in the 4th month was 0.88 mm, in the 5th – 1.09 mm, the 6th – 1.87 mm, the 7th – 2.1 mm, and the 8th – 2.35 mm. According to Szpinda [33], the right pulmonary artery diameter in the 4th month was 0.93 mm, in the 5th – 1.19 mm, the 6th – 2.05 mm, the 7th – 2.32 mm, and the 8th – 2.62 mm.

Within the entire study group, we did not find any sex related differences with respect to the dimensions of the analyzed pulmonary vessels. Also, no differences with regard to sex were reported by Firpo et al. [13], Szpinda et al. [31], and Szpinda [32, 33]. Similar conclusions were reached by Schulz and Giordano [29] in their study concerning fetuses and newborns (526 subjects). Other studies on cardiovascular embryology also failed to show any sex related differences [22, 23, 25, 26]. However, Malinowski et al. [22, 23] found female fetuses to have slightly larger vessel diameters, which he then explained to be as a result of accelerated organogenesis in females. Such an explanation would justify the larger pulmonary trunk and the left pulmonary artery diameters found in females in the 5th and 6th months of prenatal life respectively (Tab. 1, 3).

CONCLUSIONS

1. Growth with respect to the diameters of the pulmonary trunk and arteries is linear in time.
2. These dimensions do not differ between the sexes.
3. The left pulmonary artery is smaller than the right pulmonary artery.

REFERENCES

1. Achiron R., Golan-Porat N., Gabbay U., Rotstein Z., Heggesh J., Mashiach S., Lipitz S.: *In utero ultrasonographic measurements of fetal aortic and pulmonary artery diameters during the first half of gestation*. *Ultrasound Obstet. Gynecol.*, 1998; 11 (3): 180–184.
2. Allan L. D., Cook A.: *Pulmonary atresia with intact ventricular septum in the fetus*. *Cardiol. Young*, 1992, 2: 367–376.
3. Allan L. D., Cook A. C., Huggon I. C. (eds.): *Fetal Echocardiography: a practical guide*. Cambridge University Press, London, 2009.
4. Alvarez L., Aránega A., Saucedo R., López F., Aránega A. E., Muros M. A.: *Morphometric data on the arterial duct in the human fetal heart*. *Int. J. Cardiol.*, 1991; 31 (3): 337–344.
5. Patterson A. S. (ed.): *Radiology of congenital heart disease*. Mosby–Year Book, St Luis, 1993.
6. Angelini A., Allan L. D., Anderson R. H., Crawford D. C., Chita S. K., Ho S. Y.: *Measurements of the dimensions of the aortic and pulmonary pathways in the human fetus: a correlative echocardiographic and morphometric study*. *Br. Heart J.* 1988; 60 (3): 221–226.
7. Cartier M. S., Doubilet P. M.: *Fetal aortic and pulmonary artery diameters: sonographic measurements in growth-retarded fetuses*. *Am. J. Roentgenol.*, 1988; 151 (5): 991–993.
8. Castañeda A. R., Jonas R. A., Mayer J. E., Hanley F. L. (eds.): *Cardiac surgery of the neonate and infant*. Saunders, Philadelphia, 1994.
9. Castillo E. H., Arteaga-Martínez M., García-Peláez I., Villasis-Keever M. A., Aguirre O. M., Morán V., Vizcaino A.: *Morphometric study of the human fetal heart. I. Arterial segment*. *Clin Anat*, 2005; 18 (4): 260–268.
10. Chaoui R., Heling K. S., Bollmann R.: *Sonographische Messungen der Durchmesser der Aorta und des Truncus pulmonalis beim Feten [Sonographic measurements of diameter of the aorta and the pulmonary in the fetus]*. *Gynäkolog Geburtsh. Rundsch*, 1994; 34: 145–151.
11. Comstock C. H., Riggs T., Lee W., Kirk J.: *Pulmonary-to-aorta diameter ratio in the normal and abnormal fetal heart*. *Am. J. Obstet. Gynecol.*, 1991; 165: 1038–1044.
12. Daubeney P. E., Sharland G. K., Cook A. C., Keeton B. R., Anderson R. H., Webber S. A.: *Pulmonary atresia with intact ventricular septum: impact of fetal echocardiography on incidence at birth and postnatal outcome*. *Circulation*, 1998; 98 (6): 562–566.

13. Firpo C., Hoffman J., Silverman N. H.: *Evaluation of fetal heart dimensions from 12 weeks to term*. Am. J. Cardiol., 2001; 87 (5): 594–600.
14. Freedom R. M., Benson L. N., Smallhorn J. F. (eds.): *Neonatal heart disease*. Springer, Berlin–Heidelberg–New York, 1992.
15. Gembruch U., Shi C., Smrcek J. M.: *Biometry of the fetal heart between 10 and 17 weeks of gestation*. Fetal Diagn. Ther., 2000; 15 (1): 20–31.
16. Hofstetter R., Engelhardt W., Prünke K., Rother A., von Bernuth G.: *Sektorechokardiographische Durchmesserbestimmung der herznahen grossen Arterien bei Kindern [Sector echocardiographic determination of the diameter of the large arteries of the heart in children]*. Z. Kardiol., 1987; 76 (1), 38–43.
17. Hornberger L. K., Sanders S. P., Sahn D. J., Rice M. J., Spevak P. J., Benacerraf B. R., McDonald R. W., Colan S. D.: *In utero pulmonary artery and aortic growth and potential for progression of pulmonary outflow tract obstruction in tetralogy of Fallot*. J. Am. Coll. Cardiol., 1995; 25 (3): 739–45.
18. Hyett J., Moscoso G., Nicolaides K.: *Morphometric analysis of the great vessels in early fetal life*. Hum. Reprod., 1995; 10 (11): 3045–3048.
19. Jakobovits A., Westlake W., Iffy L., Wingate M. B., Caterini H., Kanofsky P., Menduke H.: *Early intrauterine development. I. The rate of growth of Caucasian embryos and fetuses between the 6th and 20th weeks of gestation*. Pediatrics, 1975; 56 (2): 173–186.
20. Maciejewski R., Jarosz M., Golan J.: *Pulmonary arteries dimensions and their dependences on the age, the height and body weight*. Folia Morphol., 1992; 51 (1): 61–68.
21. Maeno Y. V., Boutin C., Hornberger L. K., McCrindle B. W., Cavallé-Garrido T., Gladman G., Smallhorn J. F.: *Prenatal diagnosis of right ventricular outflow tract obstruction with intact ventricular septum, and detection of ventriculoumonary connections*. Heart, 1999; 81 (6): 661–668.
22. Malinowski A., Kłosin R., Rucka A.: *Ciężar narządów wewnętrznych i wymiary serca u płodów żywo i martwo urodzonych [The weight of internal organs and dimensions of the heart in live and stillborn fetuses]*. Monografie AWF, Poznań, 1999, 25–61.
23. Malinowski A., Kłosin R., Rucka A.: *Somatometria płodów żywo i martwo urodzonych. Różnicowanie morfologiczne człowieka [Somatometry of live and stillborn fetuses. Human morphological development]*. Monografie AWF, Poznań, 1999, 69–99.
24. Mandarim-de-Lacerda C. A.: *Morphometry of the human heart in the second and third trimesters of gestation*. Early Hum. Dev., 1993; 35 (3): 173–182.
25. Marecki B.: *Developmental relation between the weight of internal organs and somatic features of fetuses and newborns*. Z. Morphol. Anthropol., 1989; 78 (1): 105–115.
26. Marecki B.: *Sexual dimorphism of the weight of internal organs in fetal ontogenesis*. Anthropol. Anz., 1989; 47(2): 175–184.
27. Orlandini G. E., Ruggiero C., Orlandini S. Z.: *The corrected circumference of human pulmonary trunk and arteries in relation to the size of aorta and principal bronchi*. Anat. Anz., 1986; 162 (4): 251–257.
28. Respondek-Liberska M. (ed.): *Kardiologia prenatalna dla położników i kardiologów dziecięcych [Prenatal cardiology for obstetricians and pediatric cardiologists]*. Wydawnictwo Czelej, Lublin, 2006.
29. Schulz D. M., Giordano D. A.: *Hearts of infants and children. Weights and measurements*. Archiv. Pathol., 1962; 74: 464–471.
30. Sievers H. H., Onnasch D. G., Lange P. E., Bernhard A., Heintzen P. H.: *Dimensions of the great arteries, semilunar valve roots, and right ventricular outflow tract during growth: normative angiocardio-graphic data*. Pediatr. Cardiol., 1983; 4 (3): 189–196.
31. Szpinda M., Brazis P., Elminowska-Wenda G., Wiśniewski M.: *Morphometric study of the aortic and great pulmonary arterial pathways in human fetuses*. Ann. Anat., 2006; 188 (1): 25–31.
32. Szpinda M.: *External diameters of the pulmonary arteries in human fetuses: an anatomical, digital and statistical study*. Folia Morphol., 2008; 67 (4): 240–244.
33. Szpinda M.: *The normal growth of the pulmonary trunk in human fetuses*. Folia Morphol., 2007; 66 (2): 126–130.

34. Szymankiewicz-Dangel J. (ed.): *Kardiologia płodu. Zasady diagnostyki i terapii [Fetal cardiology: diagnostics and therapy]*. OWN, Poznań, 2007.
35. Tan T.H., Heng J.T., Wong K.Y.: *Pulmonary artery diameters in premature infants: normal ranges*. Singapore Med. J., 2001; 42 (3): 102–106.
36. Tulzer G., Arzt W., Franklin R.C., Loughna P.V., Mair R., Gardiner H.M.: *Fetal pulmonary valvuloplasty for critical pulmonary stenosis or atresia with intact septum*. Lancet, 2002; 360 (9345): 1567–1568.
37. Ursell P.C., Byrne J.M., Fears T.R., Strobino B.A., Gersony W.M.: *Growth of the great vessels in the normal human fetus and in the fetus with cardiac defects*. Circulation, 1991; 84 (5): 2028–2033.
38. Yagel S., Silverman N.H., Gembruch U. (eds.): *Fetal cardiology: embryology, genetics, physiology, echocardiographic evaluation, diagnostic and perinatal management of cardiac diseases*. Informa Healthcare Publisher, London, 2008.
39. Zalel Y., Wiener Y., Gamzu R., Herman A., Schiff E., Achiron R.: *The three-vessel and tracheal view of the fetal heart: an in utero sonographic evaluation*. Prenat. Diagn., 2004; 24 (3): 174–178.