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The normal growth of the pulmonary trunk in human foetuses

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The rate of growth of the pulmonary trunk during gestation has not been sufficiently determined. The present study was performed on 128 spontaneously aborted human foetuses aged 15–34 weeks in order to compile normative data for pulmonary trunk dimensions at various gestational ages. With the use of anatomical dissection, digital-image analysis (the Leica QWin Pro 16 system) and statistical analysis (ANOVA, regression analysis) a range of measurements (length, diameter and volume) was analysed for the pulmonary trunk during gestation. No significant gender differences were found ($p > 0.05$). Growth curves were generated of the best fit for the plot for each morphometric feature against gestational age. The results obtained show a statistically significant correlation ($p < 0.001$) between the parameters examined and gestational age. Both the length and diameter of the pulmonary trunk were found to increase in a linear fashion throughout gestation. The length ranged from 3.17 ± 0.36 mm to 13.54 ± 1.39 mm, according to the linear function $y = -5.6035 + 0.5705 x \pm 0.9171$ ($r = 0.96$). The diameter ranged from 1.51 ± 0.24 mm to 5.30 ± 1.53 mm, according to the linear model $y = -1.4813 + 0.2154 x \pm 0.7452$ ($r = 0.86$). The pulmonary trunk volume ranged from 5.94 ± 2.21 mm^3 to 312.37 ± 154.34 mm^3, according to the quadratic function $y = 143.2 - 20.961 x + 0.791 x^2 \pm 63.306$ ($R^2 = 0.74$). The growth curves generated from my data may be useful as a reference for foetal echocardiographers in the detection of congenital cardiovascular abnormalities.

Key words: pulmonary trunk, length, external diameter, volume, digital-image analysis, regression analysis

INTRODUCTION

Normative data of the pulmonary trunk in human foetuses may be helpful in the prenatal diagnosis of congenital heart defects that involve discordant diameters of the great vessels [2]. Advances in the resolution of ultrasound equipment have led to a recent increase in early diagnostic examinations, including foetal echocardiography, in high risk pregnancies [8]. It is thus important to define the normal growth patterns for all cardiovascular structures in order to identify abnormal development as early as possible. Morphometric studies on the pulmonary trunk have previously been conducted in relation to its diameter only. The pulmonary trunk diameter increases in proportion to gestational age [16]. It may be a useful predictor of gestational age when growth retardation is suspected, because this diameter remains normal in most cases of intrauterine growth retardation [4]. There have been no previous reports of both the length and

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volume of the pulmonary trunk either in prenatal or postnatal life.

On the basis of data in the available literature the objectives set for the present study were to examine:

— the normal values for the length, diameter and volume of the pulmonary trunk at varying gestational ages;
— the influence of sex on the value of the parameters examined;
— the normal developmental growth of the morphometric features (growth curves).

MATERIAL AND METHODS

The examinations were carried out on 128 human foetuses of both sexes (63 male, 65 female) from spontaneous abortions or stillbirths. There was no evidence of foetal congenital cardiovascular disease. The gestational age ranged from 15 to 34 weeks (Table 1). Developmental age was determined by crown-rump length on the basis of the Iffy tables [10]. The foetuses were divided into six age groups, corresponding to the $4^{th} – 9^{th}$ months of gestation. The foetal arteries were filled with white latex LBS 3060 by means of a Stericath catheter, which was introduced by lumbar access into the abdominal aorta. The specimens were fixed by immersion in a 10% neutral formalin solution and then dissected, according to standard autopsy techniques, under a stereoscope with a Huygens ocular at a magnification of 10. The great vessels of the foetal heart were separated from the lungs, and the cardiovascular blocks were taken out of the chest cavity (Fig. 1). In each foetus the dissected pulmonary trunk was recorded with a millimetre scale using a Nikon Coolpix 8400 camera and digitalised to JPEG images. Next, the digital picture of the pulmonary trunk underwent morphometric analysis using a Leica QWin Pro 16 (Cambridge) digital-image analysis system. For each individual the following three measurements of the pulmonary trunk were made: length in mm, diameter in mm (at its midpoint), and volume in mm^3.

Table 1. Distribution of foetuses studied

Foetal age		Crown-rump length [mm]				Number	Sex	
Months	Weeks (Hbd-life)	Mean	SD	Min	Max		Male	Female
4	15	89.4	6.1	85.0	92.0	10	5	5
	16	103.7	6.1	95.0	106.0	7	3	4
5	17	114.9	8.2	111.0	121.0	6	4	2
	18	129.3	6.6	124.0	134.0	8	3	5
	19	142.7	7.7	139.0	148.0	6	3	3
	20	155.3	5.8	153.0	161.0	4	1	3
6	21	167.1	4.7	165.0	173.0	3	2	1
	22	178.1	6.9	176.0	186.0	7	4	3
	23	192.3	6.3	187.0	196.0	9	4	5
	24	202.9	5.7	199.0	207.0	11	6	5
7	25	215.2	4.8	211.0	218.0	7	5	2
	26	224.7	5.2	220.0	227.0	7	4	3
	27	234.1	4.3	231.0	237.0	4	0	4
	28	244.2	5.1	240.0	246.0	5	2	3
8	29	253.8	4.5	249.0	255.0	6	1	5
	30	262.7	3.1	260.0	264.0	6	5	1
	31	270.7	5.2	268.0	275.0	4	1	3
	32	281.4	3.7	279.0	284.0	5	4	1
9	33	290.3	6.1	286.0	293.0	9	4	5
	34	301.4	3.2	296.0	302.0	4	2	2
Total						128	63	65

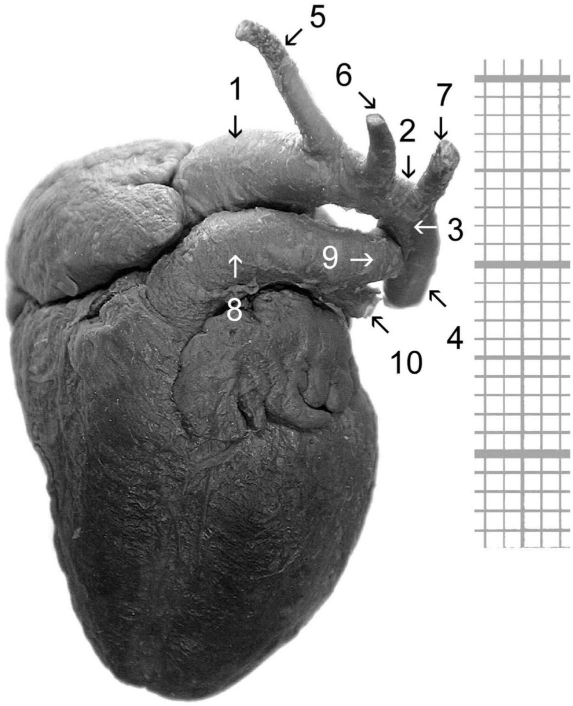

Figure 1. The great arteries of the foetal heart in a male foetus aged 23 weeks. 1 — ascending aorta, 2 — aortic arch, 3 — aortic isthmus, 4 — thoracic aorta, 5 — brachiocephalic trunk, 6 — left common carotid artery, 7 — left subclavian artery, 8 — pulmonary trunk, 9 — ductus arteriosus, 10 — left pulmonary artery.

The length, diameter and volume of the pulmonary trunk were correlated to foetal age so as to establish their growth. The results obtained were evaluated by the one-way ANOVA test for unpaired data and a *post hoc* RIR Tukey test. Regression analysis was used to derive the growth curves of best fit for the plot for each morphometric feature against gestational age. Correlation coefficients (r) between length or diameter and gestational age and the correlation of determination (R^2) between volume and gestational age were estimated.

RESULTS

Statistical analysis of the morphometric features of the pulmonary trunk showed no gender difference ($p > 0.05$). The morphometric values obtained have been presented in Table 2 without regard to sex. My findings show a statistically significant correlation ($p < 0.001$) between the parameters examined and gestational age. Figures 2–4 show the growth curves of the parameters examined of the pulmonary trunk plotted against the gestational age, together with the appropriate correlation coefficients, the lines of best fit and the 3rd and 97th percentile lines. During the study period both the length and diameter of the pulmonary trunk progressed in linear fashion with advancing gestational age. The values for pulmonary trunk length ranged from 3.17 ± ± 0.36 mm for the 4th month to 13.54 ± 1.39 mm for the 9th month of gestation. With regard to foetal age, pulmonary trunk length increased according to the linear function $y = -5.6035 + 0.5705 x \pm 0.9171$, with a correlation coefficient $r = 0.96$ (Fig. 2). The pulmonary trunk diameter ranged from 1.51 ± 0.24 mm to 5.30 ± 1.53 mm for the groups of 4 and 9 months' gestation, respectively. The pulmonary trunk diameter showed a proportional increase with advancing foetal age, according to the linear function $y = -1.4813 + 0.2154 x \pm 0.7452$ (Fig. 3). The correlation coefficient for the pulmonary trunk diameter related to gestational age reached the value $r = 0.86$. The values of the pulmonary trunk volume ranged from 5.94 ± 2.21 mm^3 to 312.37 ± 154.34 mm^3 during the study period. The volumetric growth of the pulmonary trunk was dependent on foetal age in weeks, according to the quadratic function $y = 143.2 - 20.961 x +$

Table 2. Morphometric parameters (length, diameter, volume) of the pulmonary trunk

Foetal age [month]	N	Length [mm]		Diameter [mm]		Volume [mm^3]	
		Mean	SD	Mean	SD	Mean	SD
4	17	3.17^A	0.36	1.51^G	0.24	5.94^a	2.21
5	24	4.90^B	0.91	2.44^{H,I}	0.44	23.97^a	10.03
6	30	7.52^C	0.95	3.79^J	0.43	86.72^b	25.60
7	23	9.31^D	1.17	4.16^J	0.64	127.92^{b,L}	39.34
8	21	11.65^E	1.52	5.15^K	0.95	249.57^M	96.14
9	13	13.54^F	1.39	5.30^K	1.53	312.37^N	154.34

Means for length, marked by different letters: A, B, C, D, E, F in column differ siginificantly: $p < 0.001$.
Means for diameter, marked by different letters: G, H, I, J, K in column differ significantly: for G, H $p < 0.01$; for I–K $p < 0.001$.
Means for volume, marked by different letters: a, b, L, M, N in column differ significantly: for a, b $p < 0.05$; for L–N $p < 0.001$.

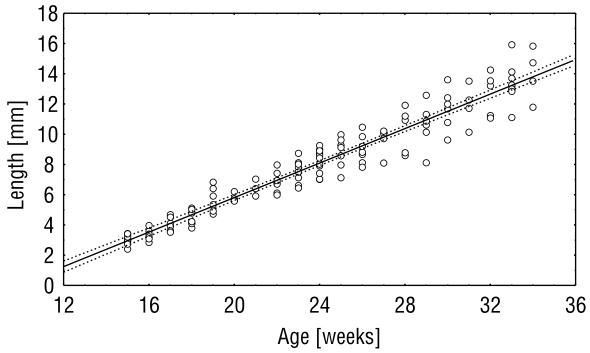

Figure 2. Regression line for the length (y) of the pulmonary trunk *vs.* gestational age (x); Length y = – 5.6035 + 0.5705 x Age ± 0.9171 (r = 0.96, p<0.001).

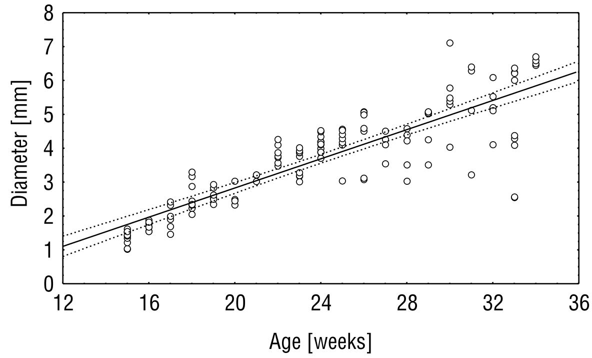

Figure 3. Regression line for the diameter (y) of the pulmonary trunk *vs.* gestational age (x); Diameter y = – 1.4813 + 0.2154 x Age ± 0.7452 (r = 0.86, p<0.001).

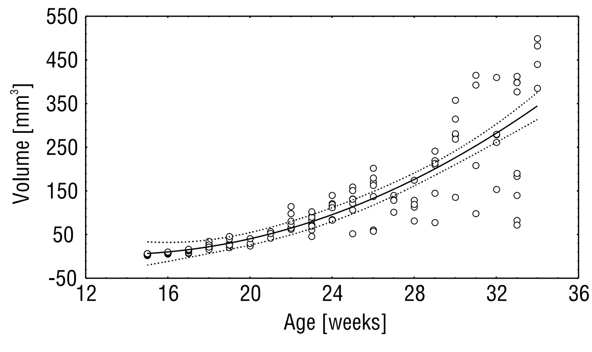

Figure 4. Regression line for the volume (y) of the pulmonary trunk *vs.* gestational age (x); Volume y = 143.2 – 20.961 x Age + 0.791 x^2 Age ± 63.306 (R^2 = 0.74).

+ 0.791 x^2 ± 63.306 (Fig. 4). The correlation of determination between the pulmonary trunk volume and foetal age reached the value $R^2 = 0.74$.

DISCUSSION

In this study the digital-image analysis system was used to provide normal dimensions for the developing pulmonary trunk at gestational ages ranging from 15 to 34 weeks. My findings confirmed the proportional growth of the pulmonary trunk diameter, that followed according to the linear function y = –1.4813 + 0.2154 x ± 0.7452. These observations are compatible with those of a previous post-mortem study from early pregnancy, which showed linear growth in the diameter of the great vessels. Hyett et al. [9] demonstrated that the pulmonary trunk diameter increased according to the regression equation: y = 0.186 – 0.892 x (r = 0.889, $p < 0.0001$). Alvarez et al. [3] found that the internal circumference of the pulmonary trunk at its origin increased by an average of 0.32 cm per kg increase in body weight, according to the regression equation y = 0.9363 + 0.3203 x (r = 0.852, $p < 0.0001$).

Echocardiographic studies have also demonstrated a linear increase in pulmonary trunk diameter (Table 3) throughout foetal life [1, 6–8, 16]. *In utero* measurements of the pulmonary trunk diameter performed by Chaoui et al. [6] showed a linear increase, according to the linear function y = –1.8 + 0.295 x (r = 0.91). Achiron et al. [1] confirmed that the pulmonary trunk diameter, measured at the level of the pulmonary valve, was expressed by the linear function y = –14.7637 + + 2.4026 x (R^2 = 0.94, $p < 0.0001$). According to Gembruch et al. [8], the pulmonary trunk diameter showed a linear increase with advancing gestational age (y = –2.69 + 0.32 x; r = 0.92, $p < 0.0001$) or biparietal diameter (y = 0.62 + 0.08 x; r = 0.93, $p < 0.0001$). Firpo et al. [7] and Zalel et al. [16] reported that the pulmonary trunk diameter was modelled as the linear functions y = –0.157 + 0.02786 x (r = 0.9081, $p < 0.01$) and y = –2.275 + 0.273 x (r = 0.93, $p < 0.0001$) respectively. Measurements of the pulmonary trunk diameter can also be used in the diagnosis of foetal intrauterine growth retardation. According to Cartier and Doubilet [4], the pulmonary trunk diameter grows normally in these foetuses.

Until now there has been no information about the length and volume of the pulmonary trunk during gestation. My measurements of the pulmonary trunk have shown that the best fit correlation between the pulmonary trunk length and the gestational age is a straight line according to the regression equation y = –5.6035 + 0.5705 x ± 0.9171 (r = 0.96, $p < 0.001$). In foetuses aged 13–20 weeks the pulmonary trunk length ranged from 4.0 mm to 8.0 mm [5]. The values of the pulmonary trunk volume generated the quadratic function y = 143.2 – 20.961 x + 0.791 x^2 ± ± 63.306. The value R^2 = 0.74 confirmed a strong relationship between the pulmonary trunk volume and gestational age. The quadratic function for arterial

Table 3. Regression equations for the pulmonary trunk diameter obtained by different authors

Author	Gestational age (weeks) (x)	Number of foetuses	Methods	Regression equation		
				Diameter [mm] (y)	r (or R^2)	p value
Hyett et al. (1995)	9–18	61	Dissection	y = 0.186 – 0.892 x	r = 0.889	p < 0.0001
My study	15–34	128		y = –1.4813 + 0.2154 x ± 0.7452	r = 0.86	p < 0.001
Chaoui et al. (1994)	20–40	157	Echocardiography	y = –1.8 + 0.295 x	r = 0.91	p < 0.001
Achiron et al. (1998)	14–26	139		y = –14.7637 + 2.4026 x	R^2 = 0.94	p < 0.0001
Gembruch et al. (2000)	10–17	136		y = –2.69 + 0.32 x	r = 0.92	p < 0.0001
Firpo et al. (2001)	12–32	164		y = –0.157 + 0.02786 x	r = 0.9081	p < 0.01
Zalel et al. (2004)	14–38	338		y = –2.275 + 0.273 x	r = 0.93	p < 0.0001

volume was applied by Szpinda et al. [15] to the volumetric growth of the brachiocephalic trunk during gestation. In the foetuses examined the pulmonary trunk volume increased 53-fold from 5.94 ± 2.21 mm^3 to 312.37 ± 154.34 mm^3. This result was obtained from the product of the length and the squared diameter, which increased approximately 4.3-fold and 3.5-fold respectively. Alvarez et al. [3] reported that the pulmonary trunk volume increased by an average of 6.4 ml per 1 ml increase in aortic isthmus volume and an average of 0.2 ml per 1 ml increase in arterial duct volume. The lack of information concerning both the length and volume of the pulmonary trunk limits discussion on this subject.

No statistically significant gender differences ($p > 0.05$) concerning the pulmonary trunk parameters were observed in the material under examination. Furthermore, in the opinion of some authors, growth of the great chest arteries in foetuses [14] and in children [11–13] has been found to be independent of gender.

The normative data for the pulmonary trunk obtained in this study provide the background for future autopsy and Doppler studies in abnormal pregnancies.

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