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The normal growth of the thoracic aorta in human foetuses

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The present study was performed on 128 spontaneously aborted human foetuses aged 15–34 weeks in order to establish normal values for thoracic aorta dimensions at various gestational ages. Using anatomical dissection, digital-image analysis (the Leica QWin Pro 16 system) and statistical analysis (ANOVA, regression analysis) the growth of the length, the original and terminal external diameters and the volume of the thoracic aorta during gestation was examined. No significant gender differences were found ($p > 0.05$). The growth curves were generated of the best fit for the plot for each morphometric feature against gestational age. Both the length and external diameters of the thoracic aorta increased in proportion to the advance in foetal age. The length ranged from 12.49 ± 1.85 mm to 48.82 ± 6.31 mm according to the linear function $y = -19.654 + 2.0512 x \pm 3.5168$. The original external diameter ranged from 1.25 ± 0.28 mm to 5.65 ± 0.48 mm according to the linear fashion $y = -2.3834 + 0.2367 x \pm 0.3850$. The terminal external diameter ranged from 1.15 ± 0.26 mm to 5.18 ± 0.45 mm, in agreement with the linear model $y = -2.1438 + 0.2156 x \pm 0.3555$ ($r = 0.96$, $p < 0.001$ for each feature). The volume of the thoracic aorta ranged from 15.75 ± 8.06 mm^3 to 1158.01 ± 301.85 mm^3 according to the quadratic function $y = 1376.2 - 154.42 x + 4.419 x^2 \pm 125.6$ ($R^2 = 0.90$). The growth curves generated from my data may be useful as a reference for foetal echocardiographers, who must distinguish abnormal from normal foetal development.

Key words: thoracic aorta, length, external diameter, volume, digital-image analysis, regression analysis

INTRODUCTION

Until now only the diameter of the foetal thoracic aorta has been discussed in echocardiographic and anatomical studies. The vast majority of the authors have emphasised its linear increase during gestation [3, 5, 20]. Detailed examination of the diameter of the thoracic aorta in human foetuses has been obtained by foetal echocardiography [4, 13]. Veille and Sivakoff [21] found that growth-retarded human foetuses had smaller thoracic aorta diameters than did foetuses of normal growth. However, when the diameter of the thoracic aorta in the growth-retarded foetuses was corrected for estimated foetal weight, it was found to be of comparable size to those of normal foetuses. Some authors [12, 14, 15] have found cine-angiographically in neonates that the thoracic aorta had a proximal diameter similar to that of the ascending aorta. Others have reported that in foetuses [2, 17] and in infants [7, 11] the diameter of the thoracic aorta was significantly smaller

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than that of the ascending aorta. There have been no previous reports of both the length and volume of the thoracic aorta in human foetuses. The present study was undertaken in order to construct a normal range for the morphometric features of the thoracic aorta during gestation.

The aims of the study have been to examine the following:
- the normal values for the length, the original and terminal external diameters and the volume of the thoracic aorta at varying gestational ages;
- the influence of sex on the value of the features examined;
- the normal developmental growth of the morphometric features (growth curves).

MATERIAL AND METHODS

The material examined consisted of 128 human foetuses of both sexes (63 males, 65 females) from spontaneous abortions or stillbirths. The gestational age ranged from 15 to 34 weeks (Table 1). The present study was approved by the University Research Ethics Committee (statement of ethical approval KB/217/2006). In no case was the cause of foetal death related to congenital cardiovascular or non-cardiovascular anomalies. Foetal age was calculated from the measurement of crown-rump (CR) length on the basis of the Iffy tables [6]. Foetuses were grouped into six monthly cohorts, 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 (with a diameter of 0.5–1 mm), which was introduced by lumbar access into the abdominal aorta. The arterial bed filling was performed under a controlled pressure of 50–60 mm Hg with the use of a syringe infusion pump SEP 11S (Ascor S.A., Medical Equipment, Warsaw 2001). The specimens were immersed in a 10% neutral formalin solution for 4–24 months for preservation and then dissected under a stereoscope with a Huygens ocular at a magnification of 10 (Fig. 1). In each foetus the dissected thoracic aorta was placed with

Table 1. Age, number and sex of foetuses examined

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

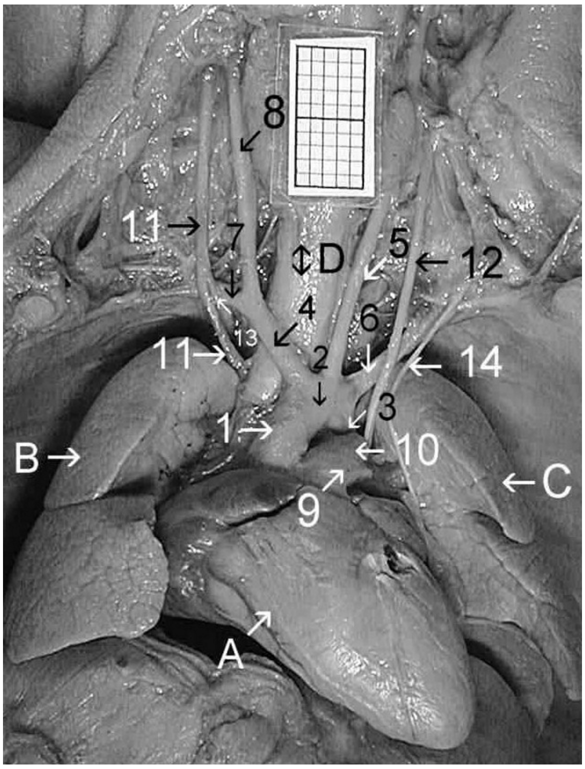

Figure 1. The great chest arteries (*in situ*) in a male foetus aged 26 weeks (*aspectus anterior*). A — heart, B — right lung, C — left lung, D — trachea, 1 — ascending aorta, 2 — aortic arch, 3 — aortic isthmus, 4 — brachiocephalic trunk, 5 — left common carotid artery, 6 — left subclavian artery, 7 — right subclavian artery, 8 — right common carotid artery, 9 — pulmonary trunk, 10 — ductus arteriosus, 11 — right vagus nerve, 12 — left vagus nerve, 13 — right recurrent laryngeal nerve, 14 — left phrenic nerve.

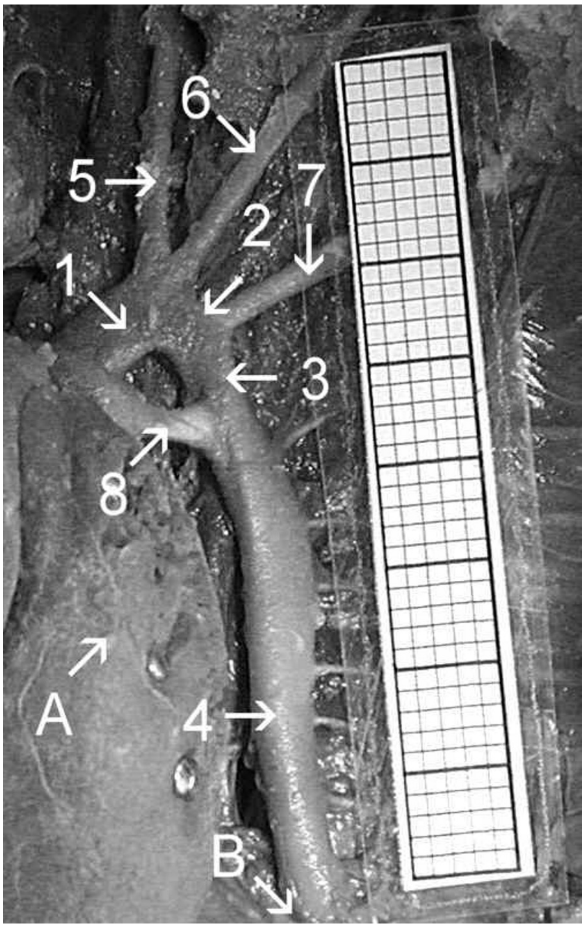

Figure 2. The great chest arteries (*in situ*) in a female foetus aged 18 weeks (*aspectus lateralis*). A — left lung, B — aortic hiatus of the diaphragm, 1 — ascending aorta, 2 — aortic arch, 3 — aortic isthmus, 4 — thoracic aorta, 5 — brachiocephalic trunk, 6 — left common carotid artery, 7 — left subclavian artery, 8 — ductus arteriosus.

a millimetre scale perpendicular to the optical lens axis and afterwards recorded using a Nikon Coolpix 8400 camera and digitalised to JPEG images (Fig. 2). Next, digital pictures of the thoracic aorta underwent morphometric analysis using the Leica QWin Pro 16 (Cambridge) digital image analysis system, which automatically estimated the length, external diameter and volume of the marked vessel. Automatic measurements of the parameters examined were derived by assuming that the filled arteries constituted a flexible cylinder. For each foetus the four following measurements were made of the thoracic aorta: length in mm, original external diameter in mm (immediately below the ductus arteriosus), terminal external diameter in mm (at the level of the aortic hiatus of the diaphragm) and volume in mm^3. The length, external diameters and volume of the thoracic aorta 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 determine the significance of the relation between gestational age and each morphometric feature of the thoracic aorta. Correlation coefficients (r) between length or external diameters and foetal age and the coefficient of determination (R^2) between volume and foetal age were estimated. Differences were considered significant at $p < 0.05$.

RESULTS

The source pictures of the great chest arteries are presented in Figures 1–4. The statistical analysis of the morphometric features of the thoracic aorta showed no gender difference ($p > 0.05$). The morphometric values obtained have been presented

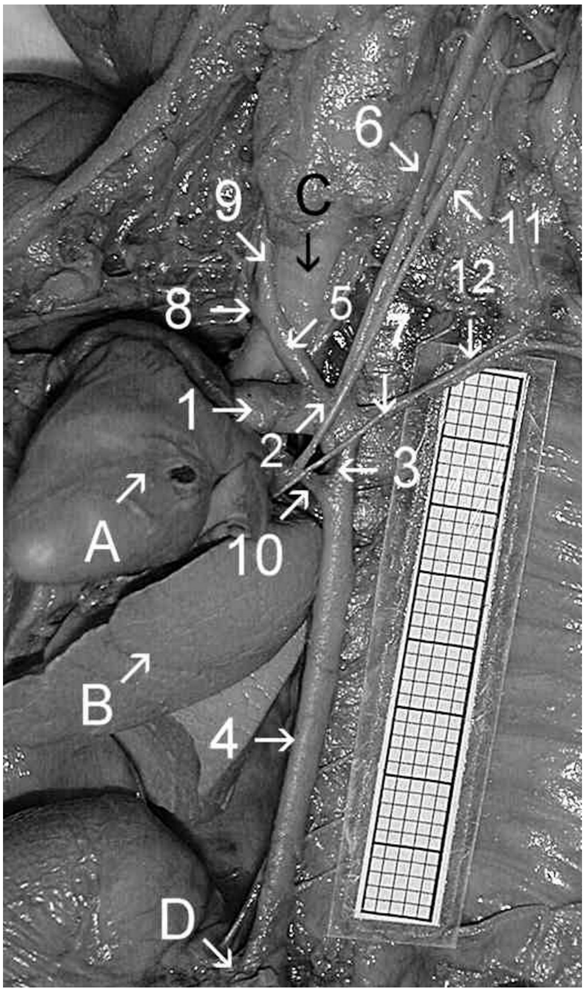

Figure 3. The great chest arteries (*in situ*) in a male foetus aged 28 weeks (*aspectus lateralis*). A — heart, B — right lung, C — trachea, D — abdominal diaphragm, 1 — ascending aorta, 2 — aortic arch, 3 — aortic isthmus, 4 — thoracic aorta, 5 — brachiocephalic trunk, 6 — left common carotid artery, 7 — left subclavian artery, 8 — right subclavian artery, 9 — right common carotid artery, 10 — ductus arteriosus, 11 — left vagus nerve, 12 — left phrenic nerve.

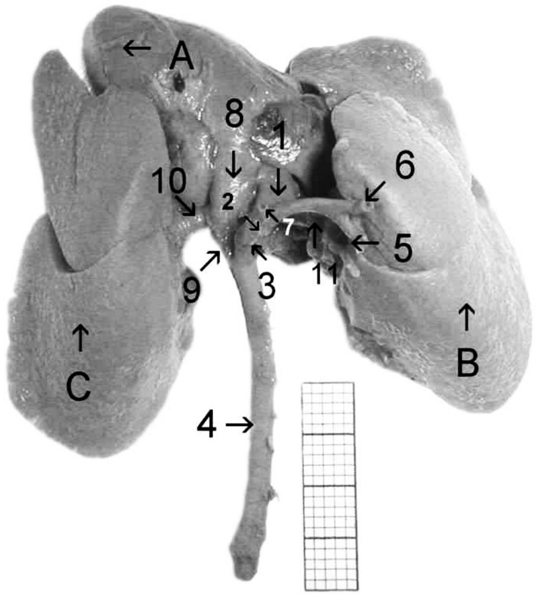

Figure 4. The great chest arteries with lungs and heart (*en block*) in a female foetus aged 27 weeks (*aspectus posterior*). A — heart, B — right lung, C — left lung, 1 — ascending aorta, 2 — aortic arch, 3 — aortic isthmus, 4 — thoracic aorta, 5 — brachiocephalic trunk, 6 — left common carotid artery, 7 — left subclavian artery, 8 — pulmonary trunk, 9 — ductus arteriosus, 10 — left pulmonary artery, 11 — right pulmonary artery.

in Table 2 without regard to sex. All four vessel features increased significantly with gestational age. The relation between the thoracic aorta parameters and gestational age is displayed in Figures 5–8, together with the appropriate correlation coefficients for length and external diameters or the coefficient of determination for volume, the curves of the best fit and the 3rd and 97th percentile lines. The 97th and 3rd percentiles for each morphometric feature at varying gestational ages were defined by the upper and lower borders respectively of the 95% confidence limits around each regression analysis.

During the period under examination both the length and external diameters of the thoracic aorta progressed in linear fashion with advancing gestational age. The values of thoracic aorta length ranged from 12.49 ± 1.85 mm for the 4th month to 48.82 ± ± 6.31 mm for the 9th month of gestation. With regard to foetal age, the length of the thoracic aorta increased according to the linear function $y = -19.654 + 2.0512\,x \pm 3.5168$, with a correlation coefficient $r = 0.96$ (Fig. 5). The results obtained were statistically significant ($p < 0.001$) for each age group. The original external diameter of the thoracic aorta ranged from 1.25 ± 0.28 mm to 5.65 ± ± 0.48 mm for the groups of 4 and 9 months' gestation, respectively. The original external diameter of the thoracic aorta showed a proportional increase with advancing foetal age, according to the linear function $y = -2.3834 + 0.2367\,x \pm 0.3850$ (Fig. 6). The terminal external diameter of the thoracic aorta ranged from 1.15 ± 0.26 mm for foetuses aged 4 months to 5.18 ± 0.45 mm for foetuses aged 9 months. The growth of the terminal external diameter of the thoracic aorta followed the linear function $y = -2.1438 + 0.2156\,x \pm 0.3555$ (Fig. 7). Correlation coefficients between both diameters of the thoracic aorta and gestational age were statistically

Table 2. Block scheme of the statistical analysis of the thoracic aorta parameters

Foetal age [month]	Length [mm] (mean±SD)	Original external diameter [mm] (mean±SD)	Terminal external diameter [mm] (mean±SD)	Volume [mm³] (mean±SD)
4	12.49±1.85	1.25±0.28	1.15±0.26	15.75±8.06
	↓ (p < 0.01)	↓ (p < 0.001)	↓ (p < 0.001)	↓ (p > 0.05)
5	17.80±2.76	2.07±0.35	1.94±0.32	60.28±29.77
	↓ (p < 0.001)	↓ (p < 0.001)	↓ (p < 0.001)	↓ (p < 0.05)
6	27.46±3.42)	3.05±0.38	2.79±0.35	190.23±60.92
	↓ (p < 0.001)	↓ (p < 0.001)	↓ (p < 0.001)	↓ (p > 0.05)
7	33.02±4.07	3.62±0.55	3.33±0.52	331.16±120.56
	↓ (p < 0.001)	↓ (p < 0.001)	↓ (p < 0.001)	↓ (p < 0.001)
8	43.62±4.99	4.84±0.59	4.43±0.55	763.35±229.41
	↓ (p < 0.05)	↓ (p < 0.001)	↓ (p < 0.001)	↓ (p < 0.001)
9	48.82±6.31	5.65±0.48	5.18±0.45	1158.01±301.85

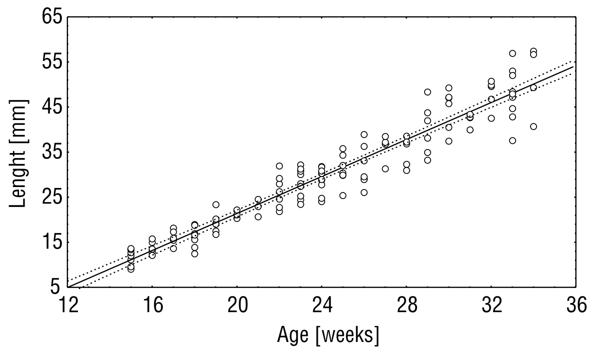

Figure 5. Regression line for the length (y) of the thoracic aorta *vs.* foetal age (x); Lenght y = –19.654 + 2.0512 x Age ± 3.5168 ($r = 0.96$, $p < 0.001$).

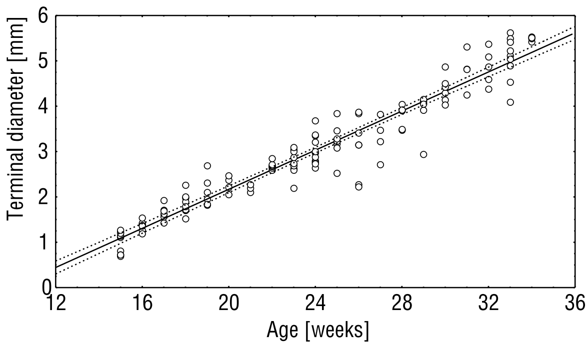

Figure 7. Regression line for the terminal external diameter (y) of the thoracic aorta *vs.* foetal age (x); Terminal diameter y = – 2.1438 + + 0.2156 x ± Age 0.3555 ($r = 0.96$, $p < 0.001$).

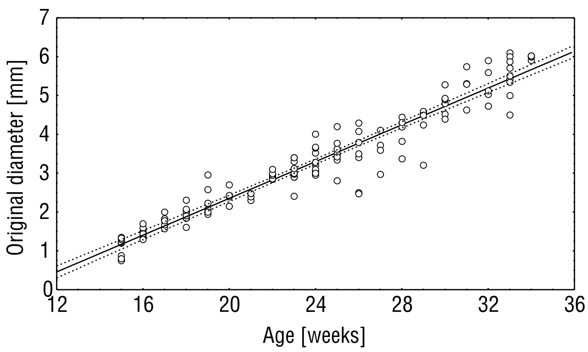

Figure 6. Regression line for the original external diameter (y) of the thoracic aorta *vs.* foetal age (x); Original diameter y = – 2.3834 + + 0.2367 x Age ± 0.3850 ($r = 0.96$, $p < 0.001$).

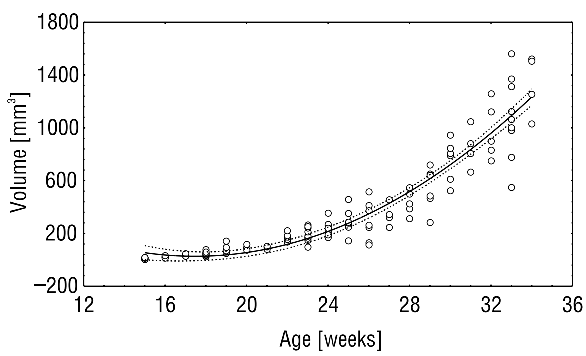

Figure 8. Regression line for the volume (y) of the thoracic aorta *vs.* foetal age (x); Volume y = 1376.2 – 154.42 x + 4.419 x^2 Age ± 125.6 ($R^2 = 0.90$).

significant ($p < 0.001$) and reached the value $r = 0.96$. The values of the thoracic aorta volume ranged from 15.75 ± 8.06 mm^3 to 1158.01 ± 301.85 mm^3 during the study period. The volumetric growth of the thoracic aorta was dependent on foetal age in weeks, according to the quadratic function $y = 1376.2 - 154.42 x + 4.419 x^2 \pm 125.6$ (Fig. 8). The coefficient of determination between volume and foetal age reached the value $R^2 = 0.90$.

DISCUSSION

Reference data for dimensions of the thoracic aorta, as determined using both echocardiography and anatomical dissection, are scarce in human foetuses. In this study the precise digital image analysis was used to provide normal morphometric parameters for the thoracic aorta during gestation. From the present data it appears that the increase in the length and diameters of the thoracic aorta is linearly related to gestational age. The values for the length of the thoracic aorta generated the linear function $y = -19.654 + 2.0512 x \pm 3.5168$. The original and terminal external diameters of the thoracic aorta also increased according to the linear model $y = -2.3834 + 0.2367 x \pm 0.3850$ and $y = -2.1438 + 0.2156 x \pm 0.3555$ respectively. It should be noted that the positive correlation coefficients of these parameters with foetal age were highly significant ($p < 0.001$) and reached the value $r = 0.96$ for each parameter. The linear growth of the thoracic aorta diameter is consistent with some post-mortem observations [1, 5, 7] and echocardiographic study [3]. According to van Meurs-van Woezik and Krediet [7], the approximately five-fold increase in body length, from 30 to 140 cm, was accompanied by a parallel increase in the original diameter of the thoracic aorta from 3.5 mm to 14.5 mm, according to the regression line $y = 1.181 + 0.90 x$. Similarly, Hyett et al. [5] reported that in foetuses aged 9–18 weeks of gestation an increase in the original diameter of the thoracic aorta was expressed by the regression equation $y = 0.16 - 0.972 x$ ($r = 0.917$, $p < 0.0001$). Firpo et al. [3], by *in utero* ultrasonographic study, confirmed the regression equation for the original diameters of the thoracic aorta as a function of gestational age $y = -0.2251 + 0.032349 x - 0.00029 x^2$ ($r = 0.8945$, $p < 0.001$). Alvarez et al. [1] found that the internal circumference of the thoracic aorta, at a point 1 cm distal to the anastomosis of the arterial duct, ranged from 1.078 cm in foetuses weighing 101 g to 1.854 cm in specimens weighing 5000 g. Regression plots of this parameter against body weight in kilograms demonstrated the linear equation $y = 0.7532 + 0.2498 x$ ($r = 0.88$, $p < 0.0001$). My measurements of the thoracic aorta volume clearly show its dependence on foetal age in accordance with the quadratic function $y = 1376.2 - 154.421 x + 4.419 x^2 \pm 125.63$. The coefficient of determination $R^2 = 0.90$ confirmed a strong relationship between thoracic aorta volume and foetal age. In the foetuses examined the thoracic aorta volume increased 73-fold from 15.75 ± 8.06 mm^3 to 1158.01 ± 301.85 mm^3. This result was obtained from the product of the length and the squared diameter, which increased approximately 4.0-fold and 4.5-fold respectively. The quadratic function for arterial volume was applied to the volumetric growth of the brachiocephalic trunk [16], ductus arteriosus [18] and ascending aorta [19] during gestation. The lack of information in the professional literature concerning both the length and volume of the thoracic aorta limits discussion on this subject.

A lack of statistically significant gender differences in the thoracic aorta parameters was also observed. In this aspect my results are in accordance with the findings of some other authors [8–10].

In this study I have characterised the growth pattern of the thoracic aorta in foetuses from 15 to 34 weeks of gestation. The growth curves generated from my data may be useful as a reference for foetal echocardiographers, who must distinguish abnormal from normal foetal development.

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