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CORRELATION BETWEEN ASCENDING AORTA, PULMONARY TRUNK, AND BRACHIOCEPHALIC TRUNK DIAMETERS DURING FETAL DEVELOPMENT

Felipe Matheus Sant'Anna Aragão¹, Iapunira Catarina Sant'Anna Aragão², Marcelo Lucas de Lima Prado³, Bárbara Costa Lourenço⁴, Vera Lúcia Correa Feitosa⁵, Francisco Prado Reis⁶, Danilo Ribeiro Guerra⁷, Deise Maria Furtado de Mendonça⁸, José Aderval Aragão⁹



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ORIGINAL STUDY

RESUMO

Introdução: A morfometria vascular desempenha um papel fundamental no diagnóstico de patologias congênitas e no suporte ao manejo clínico. Embora os diâmetros dos grandes vasos em adultos sejam bem estabelecidos, com influências de fatores como idade e sexo, ainda existe uma lacuna na literatura em relação ao seu desenvolvimento em fetos. Em particular, a relação entre os diâmetros da aorta ascendente (AA), tronco pulmonar (TP) e tronco braquiocéfálico (TBC) com a idade gestacional e o sexo, bem como o início do dimorfismo sexual ao longo do desenvolvimento, permanece inexplorada. **Objetivo:** Investigar a correlação entre os diâmetros da AA, TP e TBC com a idade gestacional e o sexo em fetos humanos. **Metodologia:** Trinta e cinco cadáveres fetais (18 masculinos, 17 femininos), coletados entre 2012 e 2020 no Laboratório de Anatomia Humana da UFS, foram analisados após aprovação ética e exclusão de malformações cardiovasculares. A idade gestacional foi determinada utilizando o método do comprimento hálux-calcâneo. Os diâmetros externos da AA, TP e TBC foram medidos com um paquímetro digital. Os dados foram analisados utilizando o coeficiente de correlação de Spearman para avaliar associações com a idade gestacional e o teste t de Student para comparar diferenças entre os sexos. **Resultados:** Foram encontradas fortes correlações positivas entre a idade gestacional e os diâmetros da AA ($p = 0,710$), TP ($p = 0,701$) e TBC ($p = 0,828$) ($p < 0,001$ para todos), confirmando um crescimento consistente ao longo do desenvolvimento fetal. Nenhuma diferença significativa foi encontrada entre sexos masculino e feminino ($p > 0,05$). **Conclusão:** Este estudo fornece dados normativos fetais para a AA, TP e TBC, demonstrando que os diâmetros dos vasos aumentam proporcionalmente com a idade gestacional. A ausência de dimorfismo sexual no período fetal sugere que fatores hormonais e ambientais pós-natais podem contribuir para as diferenças de tamanho vascular observadas mais tarde na vida. Essas descobertas fornecem valores de referência clinicamente relevantes para o diagnóstico pré-natal

de anormalidades vasculares. Além disso, aprimoram a compreensão do desenvolvimento vascular.

Palavras-chave: Biometria Vascular; desenvolvimento fetal; Arco Aórtico; Artéria Inominada; Doenças e Anormalidades Neonatais; Aorta Ascendente; Tronco Braquiocefálico; Diâmetro Externo.

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ABSTRACT

Introduction: Vascular morphometry plays a key role in diagnosing congenital pathologies and supporting clinical management. Although the diameters of great vessels in adults are well-established, with influences from factors such as age and sex, there remains a gap in the literature regarding their development in fetuses. In particular, the relationship between the diameters of the ascending aorta (AA), pulmonary trunk (PT), and brachiocephalic trunk (BCT) with gestational age and sex, as well as the onset of sexual dimorphism throughout development, remains underexplored. **Objective:** To investigate the correlation between the diameters of the AA, PT, and BCT with gestational age and sex in human fetuses. **Methodology:** Thirty-five fetal cadavers (18 male, 17 female), collected between 2012 and 2020 at the Human Anatomy Laboratory of UFS, were analyzed following ethical approval and exclusion of cardiovascular malformations. Gestational age was determined using the hallux-to-calcaneus length method. External diameters of the AA, PT, and BCT were measured with a digital caliper. Data were analyzed using Spearman's correlation coefficient to assess associations with gestational age and Student's t test to compare differences between sexes. **Results:** Strong positive correlations were found between gestational age and the diameters of the AA ($p = 0.710$), PT ($p = 0.701$), and BCT ($p = 0.828$) ($p < 0.001$ for all), confirming consistent growth throughout fetal development. No significant differences were found between males and females ($p > 0.05$). **Conclusion:** This study provides normative fetal data for the AA, PT, and BCT, demonstrating that vessel diameters increase proportionally with gestational age. The absence of sexual dimorphism in the fetal period suggests that postnatal hormonal and environmental factors may contribute to vascular size differences observed later in life. These findings provide clinically relevant reference values for prenatal diagnosis of vascular abnormalities. In addition, enhance understanding of vascular development.

Keywords: Vascular Biometry; Fetal development; Aortic Arch; Innominate Artery; Neonatal Diseases and Abnormalities; Ascending Aorta; Brachiocephalic Trunk; External Diameter.

Affiliated institution

1 Cardiology Resident at the Heart Institute of the Hospital das Clínicas, Faculty of Medicine, University of São Paulo (INCOR), São Paulo, SP, Brazil.

2 Medical Clinic of Municipal Hospital Munir Rafful (MHMR), Volta Redonda, Rio de Janeiro, Brazil.

3 Medical Student, Department of Medicine, Federal University of Sergipe (UFS), Aracaju, Sergipe, Brazil.

4 General Surgery Resident at Getúlio Vargas Hospital, Rio de Janeiro, RJ, Brazil.

5 Titular Professor of Molecular Biology, Federal University of Sergipe (UFS), Aracaju, Sergipe, Brazil.

6 Titular Professor of the Medical School, Tiradentes University (UNIT), Aracaju, Sergipe, Brazil

7 Associate Professor of Anatomy, Department of Morphology, Federal University of Sergipe (UFS), Aracaju, Sergipe, Brazil.

8 Associate Professor of Anatomy, Department of Morphology, Federal University of Sergipe (UFS), Aracaju, Sergipe, Brazil.

9 Titular Professor of Clinical Anatomy, Department of Morphology, Federal University of Sergipe (UFS), Aracaju, Sergipe, Brazil.

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INTRODUCTION

A detailed understanding of vascular morphometry is a fundamental pillar in cardiovascular medicine, guiding everything from the assessment of fetal development and early diagnosis of congenital pathologies to risk stratification and surgical planning in adults.^{1,2} Anomalies in the diameters of great vessels, such as the aorta and pulmonary arteries, can be indicative of serious conditions like aortic syndromes, pulmonary hypertension, or congenital heart diseases, underscoring the critical need for precise and contextualized reference values across all age groups.

The ascending aorta (AA), in particular, has been extensively investigated due to its relevance in aortic dilation and the risk of acute dissection.^{2,3} In adults, factors such as age, male sex, and body surface area (BSA) emerge as robust and independent predictors of AA diameter. Rogers et al.,⁴ deepened this understanding by providing detailed prediction formulas for aortic diameters adjusted for age, sex, and BSA, based on data from the Framingham Heart Study. Jappar et al.,³ reinforced the importance of specific population-based reference values, observing that AA diameter in Asian adults is generally smaller, with age and BSA being more significant predictors than traditional cardiovascular risk factors. However, Sievers and Charitos,² warn that exclusive reliance on fixed diameter thresholds for surgical indication is insufficient, given that a considerable proportion of acute dissections occur in aortas with diameters considered "normal," advocating for a more individualized assessment that integrates multiple risk factors. Kaplan et al.,⁵ compared the efficacy of echocardiography with computed tomography (CT) in detecting enlarged AA, showing that while both modalities identify a similar prevalence of dilation, echocardiography may underestimate larger aneurysms,

highlighting the relevance of appropriate imaging methodology selection. In the context of congenital pathology, Ilbawi et al.,¹ revealed severe hypoplasia and tissue folds in the ascending aorta of patients with Hypoplastic Left Heart Syndrome, emphasizing the drastic impact of fetal hemodynamic anomalies on vascular morphometry.

The pulmonary trunk (PT) and its pulmonary arteries (PAs) are also vitally important vessels, and their diameters are key indicators of conditions such as pulmonary hypertension.^{6,7} Defining a "normal" PT diameter has historically been challenging, with Ring⁸ pointing out the scarcity and inconsistency of reference values reported across different imaging modalities. This author, along with Wittram,⁹ advocated for more comprehensive studies correlating PT diameters with demonstrably normal pulmonary pressures, adjusted for variables such as age, sex, height, and body surface area. Shen et al.,⁶ in a meta-analysis, validated the use of CT for measuring PT diameter in detecting pulmonary hypertension but highlighted significant heterogeneity among studies and wide variation in diagnostic cut-off points. Sarikaya et al.,¹⁰ added a layer of complexity by demonstrating that PT diameter varies significantly during the cardiac cycle (with an average difference of 3.5 mm between systole and diastole), suggesting that unsynchronized measurements can lead to erroneous interpretations. Although this PT variation did not show significant dependence on sex or age in healthy adults, the PT/AA ratio variation was greater in women. Regarding pathology, Xiao et al.,¹¹ presented a case of pulmonary trunk stenosis post-lung transplantation, illustrating the anatomical and hemodynamic consequences of organ size disparity and the relevance of vascular diameter for intervention. Thijssen et al.,¹² provided valuable longitudinal data, demonstrating that the increase in thoracic aortic diameters is a normal process with aging, but at slower rates than previously assumed. Williams,¹³ highlighted that thoracic

aortic diameters, obtained by non-contrast CT, are independent predictors of all-cause mortality in both sexes, but, crucially, are predictors of cardiovascular mortality and stroke only in women.

In contrast to the abundance of data on adults, fetal vascular morphometry, especially in an integrated context that simultaneously evaluates multiple great vessels and their correlation with age and sex, remains less explored. Studies focused on the fetal development of specific vessels, such as those by Szpinda¹⁴ on the AA, Szpinda¹⁵ on the PT, and Szpinda¹⁶ on the pulmonary arteries, revealed linear growth in diameters and lengths, and quadratic growth in volume, all strongly correlated with gestational age. A consistently notable finding in these fetal studies is the absence of significant differences in vascular diameters between sexes during gestation, which raises questions about when and how sexual dimorphism, so evident in adulthood, is established. The brachiocephalic trunk (BCT), a critical artery for head and upper limb irrigation, still presents a gap in detailed morphometric data, especially in specific populations. The study by Aragão et al.,¹⁷ in Brazilian fetuses contributed to filling this gap and, similarly, found no significant differences in BCT between sexes, although the authors acknowledged the limitation of not having stratified the sample by gestational age.

The literature gap thus lies in the scarcity of studies that comprehensively address the correlation of AA, BCT, and PT diameters with age and sex within a single fetal cohort. Such studies would offer a holistic view of vascular growth and the eventual emergence (or absence) of sexual dimorphism. The need for population-specific normative data, as demonstrated by studies in Asian adults and Brazilian fetuses, is equally pressing to ensure the clinical applicability of these measurements. In this context, the present study aims to analyze the morphometric relationships of the AA, PT, and BCT in human

fetuses, investigating their correlation with gestational age and potential sex-related differences. By establishing normative data for these vessels, this research seeks to provide reference values applicable to both anatomical studies and clinical practice, contributing to improved prenatal diagnostics and a deeper understanding of cardiovascular development.

METHODOLOGY

Sample

An observational study was conducted using 35 fetal cadavers, comprising 18 male and 17 female specimens. The specimens were selected by convenience and collected between 2012 and 2020. All cadavers, fixed in a 10% formalin solution, are part of the collection of the Human Anatomy Laboratory of the Morphology Department at the Federal University of Sergipe (UFS), Aracaju, SE, Brazil.

Ethical Considerations

The use of the specimens strictly followed Brazilian Federal Law No. 8.501, of November 30, 1992, which addresses the destination of unclaimed cadavers for study and research purposes. Ethical approval was obtained from the Research Ethics Committee of the Federal University of Sergipe (approval number 0383.0.107.000-11).

Inclusion and Exclusion Criteria

All fetuses available in the laboratory's collection that met the study's requirements were included. Fetuses with congenital cardiovascular malformations or other macroscopically visible thoracic anomalies were excluded.

Fetal Age Determination

Gestational age was estimated using the hallux-to-calcaneus length method, which is considered a reliable and reproducible parameter for fetal age determination.¹⁸

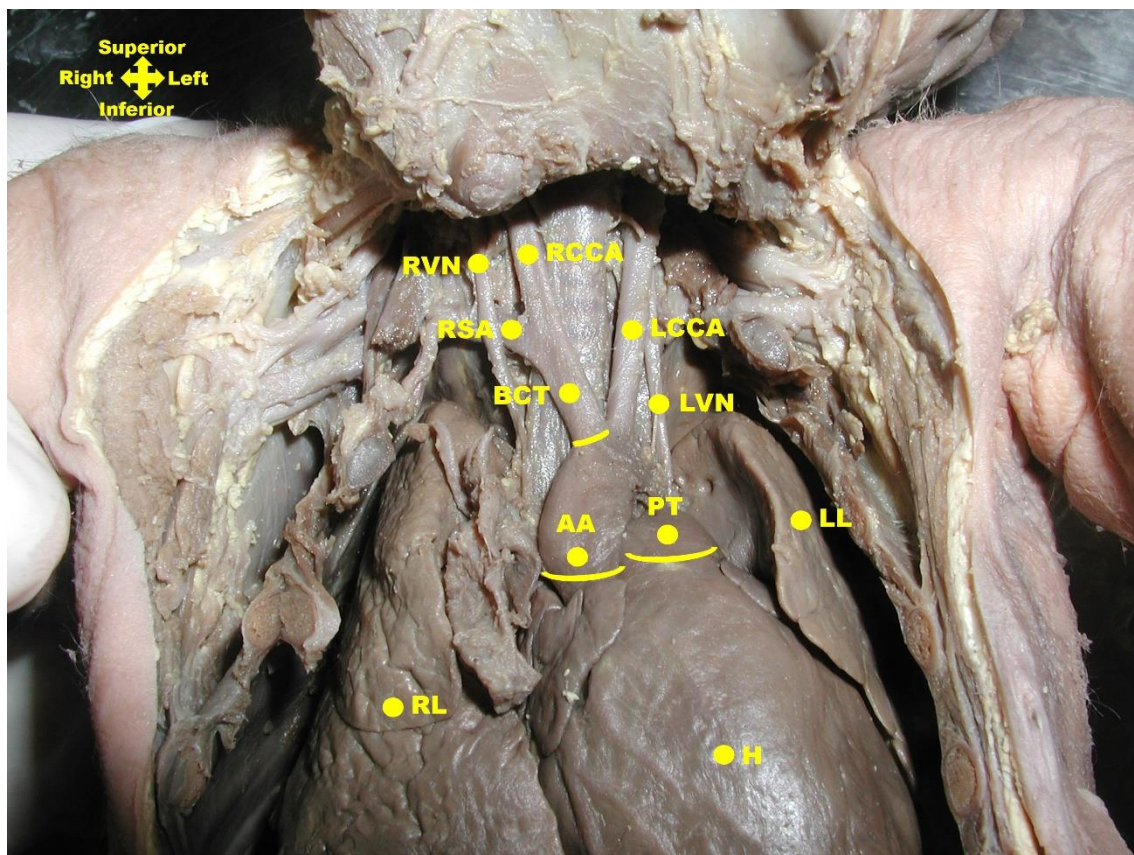
Measurements were obtained with a digital caliper, 0.05 mm precision.

Dissection and Analysis Procedure

The cadavers underwent dissection to expose the structures of interest. Initially, the anterior thoracic wall was resected. Subsequently, adipose tissue, the thymus, brachiocephalic veins, and the pericardium covering the AA and great vessels were carefully removed.

After anatomical exposure, the aortic arch, BCT, PT, and AA were individualized, and their external diameters were measured at their origin (**Figure 1**) using a digital caliper with a precision of 0.05 mm.

Figure 1. Measurements of the external diameter of AA, PT and BCT



Legend

AA - Ascending aorta; PT - Pulmonary trunk; BCT - Brachiocephalic trunk; RCCA - Right common carotid artery; LCCA - Left common carotid artery; RSA - Right subclavian artery; RVN - Right vagus nerve; LVN - Left vagus nerve; H – Heart; RL - Right lung; LL - Left lung.

All measurements were performed by two independent observers to reduce inter-observer variability. Each diameter was recorded three times, and the mean value was used for analysis.

Statistical Analysis

For variable analysis, descriptive statistics and hypothesis tests were employed. Descriptive measures, such as mean, standard deviation, median, and quartiles, were used to characterize the sample. The normality of data distribution was assessed using the Shapiro-Wilk test.¹⁹

Considering that gestational age did not exhibit a normal distribution ($p = 0.008$), Spearman's correlation was applied to investigate the association between this variable and the vascular diameters.²⁰ This coefficient ranges between -1 and 1, with values close to the extremes indicating strong correlation (negative or positive), while values close to zero suggest weak correlation. The classification adopted for the strength of correlations was: weak (0 to 0.4), moderate (0.4 to 0.7), and strong (0.7 to 1). For comparing vascular diameters between sexes, the independent samples t-test was used, as the diameters showed a normal distribution.²¹ All statistical analyses were performed using JAMOV software,²² adopting a significance level of 5% ($p < 0.05$).

RESULTS

The sample consisted of 35 fetuses (18 male and 17 female), with a mean gestational age of 25.0 ± 5.49 weeks. Among the evaluated vessels, the AA had the largest mean diameter (5.52 mm), while the BCT showed the smallest mean diameter (3.16 mm) (Table 1).

Table 1. Gestational age and diameters of major fetal vessels

	Gestational Age (weeks)	Pulmonary Trunk Diameter (mm)	Ascending Aorta Diameter (mm)	Brachiocephalic Trunk Diameter (mm)
N	35	35	35	35
Mean	25.0	4.83	5.52	3.16
Median	24.7	4.48	5.37	3.13
Standard Deviation	5.49	1.52	1.23	0.956
Minimum	18.1	2.35	3.56	1.51
Maximum	37.8	7.99	8.74	5.11
Shapiro-Wilk W	0.912	0.948	0.947	0.971
Shapiro-Wilk p	0.008	0.101	0.089	0.472
25th percentile	20.0	3.73	4.52	2.44
50th percentile	24.7	4.48	5.37	3.13
75th percentile	30.8	5.84	6.17	3.83

Sex-specific analysis revealed the same relationship of larger diameter for AA and smaller for BCT. Slightly larger mean diameters were observed in male fetuses, but these differences were not statistically significant ($p > 0.05$) for any of the vessels (Table 2).

Table 2. Gestational age and vessel diameters by sex

	Sex	Gestational Age (weeks)	Pulmonary Trunk Diameter (mm)	Ascending Aorta Diameter (mm)	Brachiocephalic Trunk Diameter (mm)
N	F	17	17	17	17
	M	18	18	18	18
Mean	F	25.0	4.87	5.45	2.99
	M	25.0	4.78	5.59	3.31
Median	F	24.7	4.48	5.35	2.86
	M	23.9	4.55	5.50	3.66
Standard Deviation	F	5.78	1.69	1.37	0.840
	M	5.38	1.38	1.11	1.05
Minimum	F	18.4	2.35	3.56	1.77
	M	18.1	2.94	4.14	1.51
Maximum	F	37.8	7.99	8.74	4.78
	M	33.1	7.15	7.54	5.11
25th percentile	F	19.9	3.76	4.50	2.53
	M	20.3	3.57	4.65	2.43
50th percentile	F	24.7	4.48	5.35	2.86
	M	23.9	4.55	5.50	3.66
75th percentile	F	27.3	5.84	6.00	3.36
	M	30.8	5.95	6.27	3.99

F - Female

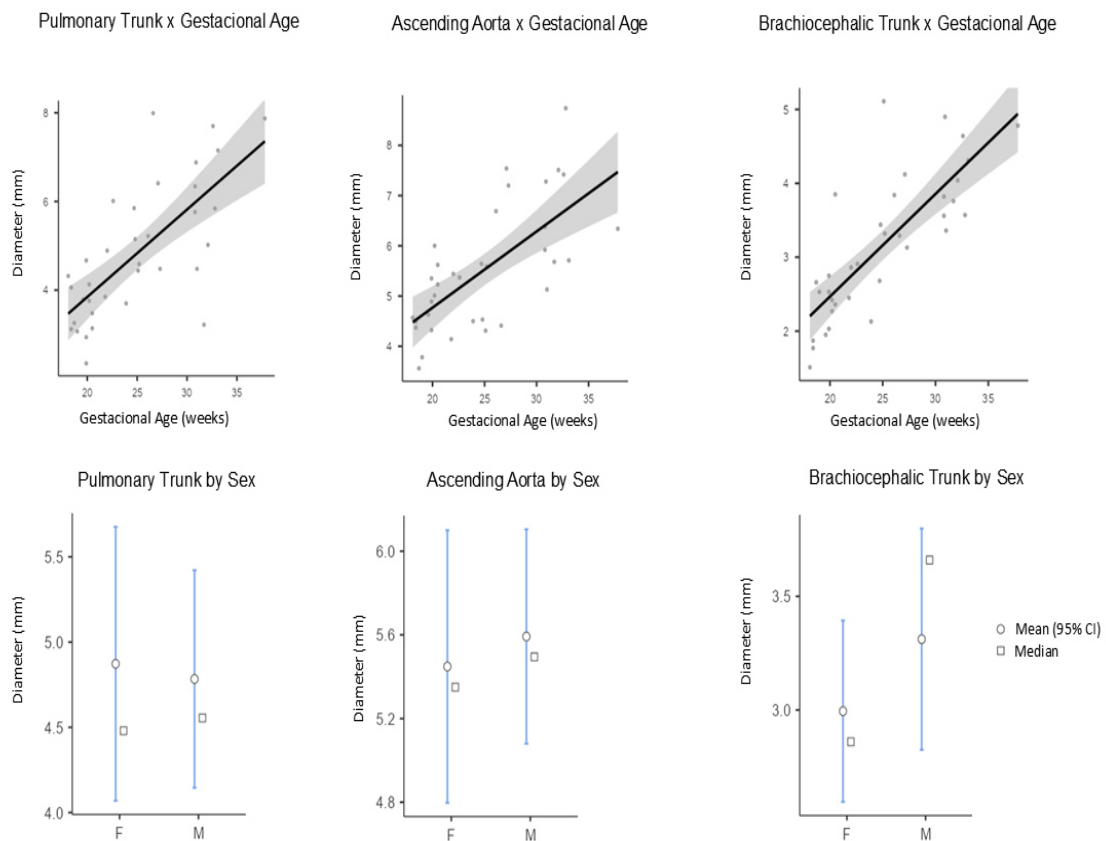
M - Male

Normality tests indicated a normal distribution for vascular diameters ($p > 0.05$), but not for gestational age ($p = 0.008$). Spearman's correlation analysis revealed a strong and significant positive association between gestational age and the diameters of the PT (p

= 0.701; $p < 0.001$), AA ($\rho = 0.710$; $p < 0.001$), and BCT ($\rho = 0.828$; $p < 0.001$) (**Figure 2**).

No significant differences were found between sexes in any of the measurements ($p > 0.05$).

Figure 2. Scatter plots showing the relationship between gestational age and diameters of PT, AA and BCT. Trend lines indicate strong positive correlations for all vessels. Box plot showing diameter differences between the sexes: no significant variation.



DISCUSSION

The study of vascular morphometry is fundamental for understanding cardiovascular development and for diagnosing congenital anomalies. In adults, the diameters of the great vessels, such as the AA, PT, and BCT, are well established and known to be influenced by variables including age, sex, and body size. These parameters provide essential benchmarks for clinical assessment and therapeutic planning.

In contrast, morphometric data on these vessels during fetal development remain scarce, despite their relevance to prenatal diagnosis and clinical management of congenital heart diseases. Accurate characterization of vascular diameters in fetuses is crucial for distinguishing physiological development from pathological alterations, especially in conditions involving aortic arch anomalies, pulmonary outflow tract obstruction, and conotruncal malformations.

This study delineates clear growth patterns of major fetal vessels and confirms the absence of sexual dimorphism during gestation. The AA showed the largest mean diameter, consistent with its central role in systemic circulation, whereas the BCT had the smallest, reflecting its function as a branch of the aortic arch.

Crucially, we observed a strong and statistically significant positive association between gestational age and the diameters of all studied vessels (PT: $p = 0.701$; AA: $p = 0.710$; BCT: $p = 0.828$; $p < 0.001$ for all). In contrast to trends observed in adult life, our study did not identify statistically significant differences in vascular diameters between sexes during the fetal period, although male fetuses exhibited subtly larger mean diameters.

The strong positive correlation between gestational age and the growth of vascular diameters is consistent with existing literature on fetal vascular development. Detailed morphometric studies conducted by Szpinda¹⁴ on the AA, Szpinda¹⁵ on the PT, and Szpinda²³ on the thoracic aorta in human fetuses also revealed linear and proportional growth of these vessels with advancing gestational age. Similarly, Szpinda¹⁶ described a linear growth of the diameters of the right and left pulmonary arteries in fetuses. These findings underscore the dynamic and continuous process of fetal cardiovascular maturation, in which the great vessels expand to accommodate the increasing blood volume and cardiac output as the fetus develops. The BCT, despite being a smaller

caliber vessel compared to the AA and PT, also exhibited robust growth strongly correlated with gestational age ($p = 0.828$), highlighting the importance of the proportional development of all components of the fetal systemic circulation.

The hierarchy of diameters observed in our study, with the AA being the largest vessel and the BCT the smallest, reflects the physiology of fetal circulation. The AA is the main vessel that distributes oxygenated blood to the systemic circulation, including the coronary arteries and aortic arch vessels, requiring an adequate diameter for high flow. The PT, although part of the pulmonary circulation, in fetal life directs most of its flow to the descending aorta through the ductus arteriosus, thus maintaining a considerable diameter.²⁴ The BCT, as one of the branches of the aortic arch, naturally has a smaller diameter compared to the main truncal vessels.

One of the most notable findings of our study was the absence of statistically significant differences in the diameters of the AA, PT, and BCT between sexes during the fetal period. This observation is consistent with several previous studies by Szpinda, who found no sexual dimorphism in the diameter of the AA,¹⁴ PT,¹⁵ or pulmonary arteries¹⁶ in human fetuses. Aragão et al.,¹⁷ also did not identify gender differences in BCT dimensions in a sample of Brazilian fetuses. This pattern contrasts sharply with what is observed in adult life, where sex emerges as an independent and significant predictor of vascular diameters. Rogers et al.,⁴ demonstrated that adult men have significantly larger absolute AA diameters than women. More recently, studies such as Thijssen et al.,¹² and Williams,¹³ indicate that, in addition to absolute diameter differences, there are sex-specific distinctions in aortic growth rates and the association between vascular diameters and cardiovascular outcomes in adults.

The transition from an absence of sexual dimorphism in fetal life to marked differences

in adulthood suggests that factors influencing these gender disparities, such as postnatal hormonal influences, different somatic growth patterns, and possibly exposure to environmental and cardiovascular risk factors throughout life, manifest predominantly after birth. The presence of subtly larger mean diameters in male fetuses in our study, though not statistically significant, may represent a very early stage of this divergence, warranting attention in future studies with greater statistical power.

From a methodological perspective, direct measurements in fetal cadavers provide high precision, minimizing variations inherent to *in vivo* imaging techniques, such as ultrasonography or magnetic resonance imaging. This approach minimizes variations inherent in measurements based on moving images or influenced by cardiac cycle phases, as demonstrated by Sarikaya et al.,¹⁰ for the PT. However, it is important to consider that post-mortem measurements may differ slightly from *in vivo* measurements due to the absence of hemodynamic pressure.

The clinical implications of our findings are significant. The availability of precise normative data on the growth of the AA, PT, and BCT in relation to gestational age is fundamental for the early diagnosis of congenital vascular anomalies, such as hypoplasia or stenosis, which may require immediate intervention. The confirmation of the absence of sexual differences in these parameters during fetal life simplifies diagnostic guidelines for this period, allowing for the use of a single set of reference values for both sexes, unlike the need for sex-adjusted values in adulthood. This knowledge can enhance healthcare professionals' ability to identify deviations from normal development and plan appropriate interventions.

A limitation of the present study is the sample size (n=35), although it is comparable to other morphometric studies on fetal cadavers. Furthermore, the absence

of a finer stratification of the sample by gestational age groups may have prevented the detection of more subtle variations in growth at specific developmental stages, a limitation acknowledged by Aragão et al.,¹⁷ in their study on the BCT. The specificity of the studied population (Brazilian human fetuses) may influence the extrapolation of results to other populations, given that population and ethnic differences have already been observed in vascular diameters.³ Future studies with larger samples, rigorously stratified by gestational age, and including diverse ethnicities, would be valuable to further enhance the understanding of fetal vascular morphometry.

CONCLUSION

Our study provides valuable normative data on the growth of the AA, PT, and BCT in human fetuses, demonstrating a strong correlation with gestational age and, crucially, the absence of sexual dimorphism in these structures during fetal life. These findings contribute significantly to the existing literature and serve as an essential basis for the diagnosis of congenital anomalies, for understanding the ontogeny of vascular sexual dimorphism, and for directing future research exploring the mechanisms underlying vascular morphological changes from fetal life to adulthood.

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