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Background:

Material/Methods:

The normal growth of cross-sectional areas of the aorto-iliac segment in human fetuses – an anatomical, digital, and statistical study

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nd: The intraluminal size of the aorto-iliac segment is relevant in both the clinical and echographic settings. The aim of this study was to compile both the absolute and relative age-specific reference intervals for cross-sectional areas (CSAs) of the aorto-iliac segment.

ds: Using the methods of anatomical dissection, digital-image analysis (Leica QWin Pro 16) and statistical analysis (Student's t test, one-way ANOVA, post-hoc RIR Tukey test, linear regression), the growth in CSA (in mm²) of the abdominal aorta, the common, external, and internal iliac arteries in 124 (60 males, 64 females) spontaneously aborted human fetuses aged 15–34 weeks was examined.

Results: No significant sex differences were found. In the age range of 4–9 months, the distal CSA of the abdominal aorta ranged from 0.87±0.34 to 19.18±3.36 mm². The CSA of the common iliac artery varied from 0.37±0.22 to 4.30±1.54 mm² on the right, and from 0.36±0.16 to 3.80±1.44 mm² on the left. The sum of the CSAs of the right and left common iliac arteries grew proportionately to the distal CSA of the abdominal aorta; the latter being significantly larger than the former. On both sides, however, the CSA of the internal iliac artery was approximately twice that of the external iliac artery. Between the ages of 4 and 9 months, the CSA of the external iliac artery ranged from 0.10±0.06 to 1.32±0.52 mm² on the right, and from 0.08±0.03 to 1.19±0.42 mm² on the left. The CSA of the internal iliac artery increased from 0.23±0.14 to 2.59±1.22 mm² on the right, and from 0.21±0.14 to 2.27±1.11 mm² on the left. Bilaterally, the sum of the CSAs of the internal and external iliac artery decreased until the age of 6 months, after which their values were gradually increasing until the age of 9 months.
Conclusions: The aorto-iliac segment does not reveal sex differences in its cross-sectional area. The cross-sectional area of the internal iliac artery is approximately twice the size of the external iliac artery. The aorto-iliac segment ob-

key words:
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served proximally to distally reduces its cross-sectional area, thereby resulting in an increase in blood velocity.

Background

The advancement of imaging techniques (USG, CT, MRI) has required an extensive knowledge of the fetal arterial development in an effort to compile both normal and pathological criteria adapted to particularities of the fetal aorto-iliac segment [1–7]. The normative morphometric data of the fetal aorto-iliac segment may be useful as age-specific reference intervals in the prenatal diagnosis and monitoring of such congenital arterial abnormalities with discordant diameters and cross-sectional areas (CSAs) as aneurysms, hypoplasia, atresia, agenesis, and idiopathic infantile arterial calcification [7–14]. These aorto-iliac malformations refer to conditions that can cause restriction to flow (aneurysms): either a severe decrease (hypoplasia, idiopathic infantile calcification) or the absence (atresia, agenesis) of aorta-iliac flux.

In the clinical and echographic settings, the intraluminal size of the aorto-iliac segment is much more relevant than its external dimensions [8,15–19]. To date, however, the existing data in the medical literature has precisely focused only on the length [8,15,16], external diameter [8,15–19], and volume [8,15,17] of the aorto-iliac segment, with no information about its luminal dimensions. The quantitative knowledge of the aorto-iliac CSAs is critical for determining the outflow-toinflow area ratios when studying the local hemodynamics [20].

In order to: 1) examine the normal growth of cross-sectional areas, and 2) hypothesize on the nature of the blood velocity in the fetal aorto-iliac segment, in the present study we aimed to:

- determine both the absolute and relative age-specific reference intervals for the CSAs of the distal part of the abdominal aorta and the proximal parts of the common, external, and internal iliac arteries, and
- examine the relationship between the CSA of the parent flow channel and the sum of the CSAs of its 2 branches.

Material and Methods

The present study was carried out on 124 ethnically homogenous human fetuses of Caucasian racial origin of both sexes (60 males, 64 females), which had been derived from spontaneous abortions or stillbirths in the years 1989–2001. Legal and ethical considerations were approved by the Research and Ethics Committee of our university (KB/217/2006). Since no malformations were identified on gross anatomical examination in all the included specimens, the diagnosis was confirmed as normal. The sample included fetuses, which were the outcome of causes of placental insufficiency. The gestational age calculated by the crown-rump length [21] varied from 15 to 34 weeks (Table 1). For statistical reasons, the fetuses were separated into 6 monthly groups, from the 4th to the 9th month of gestation. Using a syringe infusion pump SEP 11S, the arterial system was filled with white latex LBS 3060 through the abdominal aorta under a controlled pressure of 50–60 mm Hg. All specimens were immersed in 10% neutral formalin solution for 4–24 months, and then dissected anatomically. Each fetus was dissected to visualize its abdominal aorta, common, external, and internal iliac arteries (Figure 1). Afterwards, we cut 0.3 mm-thick slices in a crosssectional manner at standard levels of the aorto-iliac segment. To measure their luminal CSAs (in mm²), the slices were placed vertically to the optical lens axis, recorded using a camera (Nikon Coolpix 8400), digitalized to TIFF images (Figure 2), and finally evaluated by digital image analysis (Leica QWin Pro 16, Cambridge).

For each fetus the 7 following luminal CSAs (in mm^2) were assessed:

- 1. the distal CSA of the abdominal aorta, measured just above its bifurcation;
- 2, 3. the proximal CSAs of the right and left common iliac arteries, measured just below their origins;
- 4, 5. the proximal CSAs of the right external and internal iliac arteries, measured just below their origins;
- 6, 7. the proximal CSAs of the left external and internal iliac arteries, measured just below their origins.

In a continuous effort to minimize measurement and observer bias, all measurements were performed by 1 researcher (Sz. M.). Each measurement was repeated 3 times under the same conditions but at varying times, and the mean of the 3 was considered as definitive. The differences between the repeated measurements as the intra-observer variation were evaluated by one-way ANOVA for paired data.

Because of the different sizes of the fetuses, we expressed each luminal CSA as a ratio of the distal CSA of the abdominal aorta. As a consequence of the statistical analysis, Student's t test was applied to examine the influence of sex on the given values in each age interval. Both the absolute and relative CSAs were related to fetal age in order to express their growth dynamics. In order to test whether or not the different variables significantly changed with gestational age, the one-way ANOVA test for unpaired data and post-hoc RIR Tukey comparisons were used. Linear regression analysis was used to determine the significance of the relationship between the studied CSAs of the parent flow channel and the sum of the CSAs of its 2 branches.

Results

No significant differences were found in the evaluation of intra-observer reproducibility of the aorto-iliac measurements

Table 1. Distribution	of fetuses	studied.
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Gestatio	nal age	(Crown-rump	o length (mm)		Sex		
Months	Weeks	Mean	SD	Min.	Max	Number	Males	Females
	15	89.4	6.1	85.0	92.0	9	4	5
4	16	103.7	6.1	95.0	106.0	7	3	4
	17	114.9	8.2	111.0	121.0	5	3	2
	18	129.3	6.6	124.0	134.0	8	3	5
5	19	142.7	7.7	139.0	148.0	9	5	4
	20	155.3	5.8	153.0	161.0	2	0	2
	21	167.1	4.7	165.0	173.0	3	2	1
	22	178.1	6.9	176.0	186.0	7	4	3
6	23	192.3	6.3	187.0	196.0	9	4	5
	24	202.9	5.7	199.0	207.0	11	6	5
	25	215.2	4.8	211.0	218.0	7	5	2
	26	224.7	5.2	220.0	227.0	7	4	3
7	27	234.1	4.3	231.0	237.0	4	0	4
	28	244.2	5.1	240.0	246.0	4	2	2
	29	253.8	4.5	249.0	255.0	6	1	5
	30	262.7	3.1	260.0	264.0	6	3	3
8	31	270.7	5.2	268.0	275.0	4	1	3
	32	281.4	3.7	279.0	284.0	5	4	1
	33	290.3	6.1	286.0	293.0	7	4	3
9	34	301.4	3.2	296.0	302.0	4	2	2
Total						124	60	64

(P>0.05). The values of CSAs of the aorto-iliac segment between 2 sexes were concluded to be insignificant (P>0.05). For the afore-mentioned reason, the values obtained have been presented in Table 2, without regard to sex. On the contrary, there were significant correlations between all the CSAs studied and gestational age (P=0.0000).

The distal CSA of the abdominal aorta was the greatest value throughout gestation, ranging widely from 0.87 ± 0.34 mm² in the 4-month group to 19.18 ± 3.36 mm² in the 9-month group.

In the age range of 4–9 months, the CSA of the common iliac artery varied from 0.37 ± 0.22 to 4.30 ± 1.54 mm² on the right, and from 0.36 ± 0.16 to 3.80 ± 1.44 mm² on the left; the former, ages of 4 and 7 months excluded, was found to be significantly greater than the latter. The sum of the CSAs of the 2 common iliac arteries grew from 0.73 ± 0.36 to 8.10 ± 2.95 mm², being significantly smaller than the distal CSA of the abdominal aorta (Figure 3). During the duration of the analyzed period, the sum (y) of the CSAs of both the right and left common iliac arteries was proportionately increasing to the CSA (x) of the abdominal aorta (Figure 4), in accordance with the linear function y=-0.021+0.406 X \pm 1.507 (R²=0.71, P=0.0000).

The local aorto-iliac area ratio expressed as a quotient of the sum of the CSAs of the 2 common iliac arteries divided by the CSA of the abdominal aorta was dependent on fetal age (Figure 5A). It was found to decrease in its mean values from 0.88 to 0.35 until the age of 6 months. Afterwards, its value was gradually increasing until the age of 8 months (0.42), and finally stabilized during the 9th month.

Bilaterally, the CSA of the internal iliac artery was approximately twice that of the external iliac artery. At the age of



Figure 1. The abdominal aorta in a female fetus aged 25 weeks: A – aortic hiatus of the diaphragm, B – aortic bifurcation, 1 – abdominal aorta, 2 – right common iliac artery, 3 – left common iliac artery, 4 – right external iliac artery, 5 – right internal iliac artery, 6 – left external iliac artery, 7 – left internal iliac artery.

4 and 9 months, the CSA of the external iliac artery ranged from 0.10 ± 0.06 to 1.32 ± 0.52 mm² on the right, and from 0.08±0.03 to 1.19±0.42 mm² on the left, the former being significantly greater than the latter in the age range of 7-9 months. The CSA of the internal iliac artery increased from 0.23±0.14 to 2.59±1.22 mm² on the right, and from 0.21±0.14 to 2.27±1.11 mm² on the left, for the 4-month and 9-month groups of gestation, respectively. With the exception of the fetuses aged 4 and 7 months, the CSA of the right internal iliac artery was significantly greater than that of the left. The sum of the CSAs of the external and internal iliac arteries increased from 0.33±0.15 to 3.91±1.51 mm² on the right, and from 0.29 ± 0.17 to 3.46 ± 1.45 mm² on the left, for the 4-month and 9-month gestational groups, respectively. The growth dynamics of the CSAs studied were much more intensive in the age range of 7–9 months compared to the age of 4–6 months.

On the right (Figure 6A) and left sides (Figure 6B), the sum of the CSAs of the internal and external iliac arteries was



Figure 2. The aorto-iliac segment in cross-section in a male fetus aged 16 weeks (A), and in a female fetus aged 30 weeks (B): 1 – abdominal aorta, 2 – right common iliac artery, 3 – left common iliac artery, 4 – right external iliac artery, 5 – right internal iliac artery, 6 – left external iliac artery, 7 – left internal iliac artery.

significantly smaller than the CSA of the common iliac artery. The relationship between the sum (y) of both the CSAs of the external and internal iliac arteries in comparison to the CSA (x) of the common iliac artery was computed by the linear functions: $y=-0.069 + 0.907 \times \pm 0.187$ on the right (Figure 7A), and $y=-0.084 + 0.901 \times \pm 0.169$ on the left (R²=0.98; P=0.0000) – (Figure 7B). In the age range of 4–7 months, the common iliac bifurcation area ratio expressed as the sum of the CSAs of the external and internal iliac arteries divided by the CSA of the common iliac artery was significantly greater (P<0.01) on the right side (Figure 5B). During the 4th month, however, its value decreased, and then increased between 6 and 8 months, stabilizing in fetuses aged 9 months.

The CSAs of the 3 iliac arteries stood out in stark contrast when compared to the distal CSA of the abdominal aorta, presented as the CSA ratios (Table 2). Their relative CSAs decreased until the age of 6 months, and then gradually increased until the age of 9 months.

Discussion

Our results concerning the external dimensions (length, external diameter, volume) of the fetal aorto-iliac segment have recently been published [8,17–19]. The present paper is the first in the professional literature to highlight and accentuate the internal (luminal) CSAs of the growing aorto-iliac segment in human fetuses. This study presented a cross-sectional

nths)	tuses	Cross-sectional area (mm²) Cross-sectional area ratio														
om)	of fet	Abdominal aorta			Right iliac arteries						Left iliac arteries					
ıl age	nber			Common		External		Internal		Common		External		Internal		
Feta	Nun	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
4	16	0.87 1.00 ↓ (P<0.05)	0.34 0.00	0.37 ^A 0.43 ↓ (P>0.05)	0.22 0.12	0.10 ^c 0.11 ↓ (P>0.05)	0.06 0.03	0.23 ^E 0.26 ↓ (P>0.05)	0.14 0.06	0.36 ^A 0.41 ↓ (P>0.05)	0.16 0.03	0.08 ^D 0.09 ↓ (P>0.05)	0.03 0.02	0.21 ^E 0.24 ↓ (P>0.05)	0.14 0.08	
5	24	2.48 1.00 ↓ (P<0.05)	0.92 0.00	0.57 ^A 0.23 ↓ (P<0.05)	0.35 0.08	0.13 ^c 0.05 ↓ (P<0.05)	0.06 0.02	0.30 ^E 0.12 ↓ (P<0.05)	0.22 0.03	0.47 ^в 0.19 ↓ (P<0.05)	0.22 0.04	0.11 ^D 0.05 ↓ (P<0.05)	0.05 0.01	0.23 ^F 0.09 ↓ (P<0.05)	0.12 0.02	
6	30	5.21 1.00 ↓ (P<0.05)	1.47 0.00	0.90 ^A 0.17 ↓ (P<0.05)	0.44 0.08	0.23 ^c 0.04 ↓ (P<0.05)	0.06 0.03	0.47 [€] 0.09 ↓ (P<0.05)	0.31 0.03	0.79 ^в 0.15 ↓ (P<0.05)	0.23 0.02	0.20 ^D 0.04 ↓ (P<0.05)	0.08 0.02	0.38 ^F 0.07 ↓ (P<0.01)	0.17 0.02	
7	22	7.37 1.00 ↓ (P<0.01)	2.28 0.00	1.38 ^A 0.19 ↓ (P<0.01)	0.68 0.09	0.47 ^c 0.06 ↓ (P<0.01)	0.21 0.02	0.74 ^E 0.10 ↓ (P<0.01)	0.45 0.02	1.36 ^A 0.18 ↓ (P<0.01)	0.59 0.04	0.42 ^D 0.05 ↓ (P<0.01)	0.18 0.01	0.71 ^E 0.10 ↓ (P<0.01)	0.37 0.03	
8	21	13.08 1.00 ↓ (P<0.01)	2.97 0.00	2.90 ^A 0.22 ↓ (P<0.01)	1.55 0.11	0.91 ^c 0.07 ↓ (P<0.05)	0.41 0.02	1.62 ^E 0.12 ↓ (P<0.01)	0.85 0.03	2.65 ^B 0.20 ↓ (P<0.01)	1.33 0.03	0.79 ^c 0.06 ↓ (P<0.001)	0.24 0.01	1.48 ^F 0.11 ↓ (P<0.01)	0.91 0.02	
9	11	19.18 1.00	3.36 0.00	4.30 ^A 0.23	1.54 0.09	1.32 ^c 0.07	0.52 0.03	2.59 ^E 0.14	1.22 0.03	3.80 ^B 0.20	1.44 0.04	1.19 ^c 0.06	0.42 0.02	2.27 [⊧] 0.12	1.11 0.02	

Table 2. The statistical analysis of the cross-sectional areas of the aorto-iliac segment in human fetuses.

Means for the common iliac arteries in rows marked by different letters A and B differ significantly (P<0.05); Means for the external iliac arteries in rows marked by different letters C and D differ significantly (P<0.05); Means for the internal iliac arteries in rows marked by different letters E and F differ significantly (P<0.05).





interpretation of the longitudinal growth of 7 variables of the CSA (the distal CSA of the abdominal aorta, proximal CSAs of the right and left common iliac arteries, proximal CSAs of the right external and internal iliac arteries, and the proximal CSAs of the left external and internal iliac arteries) based on the evidence from 124 fetuses at ages of 15–34 weeks. As a result, it is not a true representation of growth of the CSA variables,



Figure 4. The sum of the cross-sectional areas of the right and left common iliac arteries *vs.* the cross-sectional area of the abdominal aorta.

but rather is a populational perspective. The main limitation of the present study seems to be that all measurements were done by 1 observer in a blind fashion.

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Figure 5. The quotient of the sum of the cross-sectional areas of the two common iliac arteries divided by the CSA of the abdominal aorta (**A**), and the sum of the cross-sectional areas of both the external and internal iliac arteries divided by the cross-sectional area of the common iliac artery *vs.* gestational age (**B**).



Figure 6. The cross-sectional areas of the common, external and internal iliac arteries on the right (A) and left (B) sides vs. gestational age.



Figure 7. The sum of the cross-sectional areas of the external and internal iliac arteries vs. the cross-sectional area of the common iliac artery on the right (A) and left (B) sides.

Because the internal borders of the examined arteries could be accurately traced in cross-section using a cursor, digital image analysis has turned out to be an excellent method of determining the luminal cross-sectional areas of the growing aorto-iliac segment. It should be emphasized that CSA calculation was based on direct measurements of the CSAs of the aorto-iliac segment in the material under examination, instead of deduced, extrapolated through a series of indirect measurements. The results obtained could be considered as both normative and real due to the 5 following reasons. Firstly, the fetuses constituted a large (n=124) sample with representation of the wide age range (4–9 months) of specimens, with no visible malformations. Secondly, the aorto-iliac segment was not affected by any arterial abnormalities such as

aneurysms, megaloaorta, hypoplasia, atresia, or idiopathic infantile arterial calcification [7,9–14]. Thirdly, a valid objective software package (Leica QWin Pro 16, Cambridge) was used for measuring luminal CSAs. Fourthly, tissue shrinkage related to formalin fixation had little (0.5–1.0%) influence on the CSAs of the aorto-iliac segment filled with latex [8,15,17–19]. Finally, the CSAs measured could be considered as precise and clearly-definable.

In agreement with the medical literature concerning external dimensions of the abdominal aorta [8,15,16], common [15–17], external and internal [16,18,19] iliac arteries in fetuses and children [22,23], in the material under examination no sex differences for the CSAs of the aorto-iliac segment were found. In adolescents and adults, however, dimensions of the aorto-iliac segment were greater in males than females of the same age [24–28].

The iliac arteries were found to be consequently larger in CSA on the right, as indicated in Table 2. However, the statistically significant differences concerning greater values of the CSAs for the right iliac arteries encompassed fetuses aged 5, 6, 8 and 9 months of the common and internal iliac arteries, and fetuses aged 4–7 months for the external iliac artery. It is paramount to notice, however, that in our series the internal iliac arteries were found to be approximately twice the CSA value in comparison with the external iliac arteries. This is because the internal iliac arteries continue as the umbilical arteries to reach the placenta.

With the exception of the lumbar and median sacral arteries, the distal abdominal aorta, the common iliac arteries, and the proximal parts of the external and internal iliac arteries do not give rise to any branches. Therefore, in terms of biophysics, this vascular region can be considered as a system of distributing channels, consisting of the primary channel (distal part of the abdominal aorta) divided twice subsequently into the 2 secondary (the right and left common iliac arteries), and the four tertiary (the right and left external and internal iliac arteries) channels of decreasing CSA values. On the basis of regression analysis, we showed that the CSA of the main flow channel turned out to be proportionate to the sum of the CSAs of its branches. Therefore, the sum of the CSAs of both the right and left common iliac arteries was increasing proportionately to the CSA of the distal abdominal aorta. In a similar manner, the sum of the CSAs of both the external and internal iliac arteries followed proportionately to the CSA of the common iliac artery. As a consequence, the total CSA of the aorto-iliac segment was found to decrease along its length proximally to distally. In fetuses aged 4 months, however, the total CSA of the aorto-iliac segment revealed a decrease in values from 0.87±0.34 mm² at the level of the distal part of the abdominal aorta, through 0.73±0.36 mm² at the level of the right and left common iliac arteries, and to 0.62±0.16 mm² at the level of the bilateral external and internal iliac arteries. Furthermore, in the 9-month group, the total CSA of the aorto-iliac segment was decreasing from 19.18±3.36 mm², through 8.10±2.95 mm², and subsequently to 7.37±1.48 mm². According to the law of continuity, the product of the CSA and its accompanying blood velocity is always constant [29,30]. Because of this, as a result of the successive decrease in the CSA found in this study, there should be a proportionate correlation between the decrease in aorto-iliac segment CSA value and the increase in its blood velocity. This means that the aorto-iliac segment, especially the common iliac arteries, must be responsible for blood acceleration. To date, however, no such hypothesis has existed in the medical literature, thereby limiting our discussion on this subject.

It has been postulated that local, individual specific arterial geometry is a potential risk factor that might result in or exaggerate atherosclerosis [31-33]. The aortic bifurcation divides the high pressure blood of the abdominal aorta into the 2 common iliac arteries. Subsequently, the bifurcation of each common iliac artery distributes blood to the lower limbs through the external iliac artery and to the pelvis through the internal iliac artery [33]. As reported by Moore et al. [32], the aorto-iliac segment is a typical site of clinically significant atherosclerosis that displays nontrivial hemodynamics expected to be sensitive to geometric variations. Due to additional disturbances in local blood flow, the aortic bifurcation and the common iliac artery bifurcations are exposed to endothelial cell damage, and thereby prone to atherosclerotic plaque formation [34,35]. According to Lallemand et al. [34], the hemodynamic stress occurs when a sufficient proportion of the pulse wave is reflected by a bifurcation, setting up a standing wave of pressure, proximal to the point of reflection (antinode). Thus, oscillatory pressure on the wall (wall shear stress) of the lower abdominal aorta or the common iliac arteries increases with percentage reflection of the pulse wave from the aortic bifurcation and the common iliac artery bifurcation, respectively [36]. As it turned out, the most important factor in determining bifurcation hemodynamics, including aorto-iliac flow, wall shear stress, and initiation of atheroma, is the outflow-to-inflow area ratio [32], defined as the ratio of the sum of the crosssectional areas of the branches divided by the cross-sectional area of the parent vessel. This ratio directly influences the amount of reflection of pulse waves arriving at a bifurcation. In the material under examination, the local aorto-iliac area ratio decreased from 0.88 to 0.35 until the age of 6 months, then gradually increased until the age of 8 months (0.42), and finally stabilized during the 9th month. In adults, the "ideal" value of the local aorto-iliac area ratio, characterized by minimum reflection of the pulse wave, is 1.15 [34,37]. From that "ideal value", both low and high ratios result in increasing wall shear stress and endothelial damage, because of increasing reflection of the pulse wave. In addition, in the present study the common iliac bifurcation area ratio decreased during 4–5 months, and then increased between 6 and 8 months, so as to stabilize in fetuses aged 9 months. In the age range of 4–7 months its value was significantly greater on the right side. To date, this area ratio has not been discussed in the professional literature.

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Conclusions

- 1. The aorto-iliac segment does not reveal sex differences in its cross-sectional area.
- 2. The cross-sectional area of the internal iliac artery is approximately twice the size of the external iliac artery.
- 3. The aorto-iliac segment, observed proximally-to-distally, reduces its cross-sectional area, thereby resulting in an increase in blood velocity.
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