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A novel formula for the classification of blood vessels according to symmetry, asymmetry and hypoplasia

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A new mathematical formula for calculating the symmetry, asymmetry and hypoplasia of blood vessel segments is presented for discussion. The study was conducted using the computed tomography (CT) files from 80 patients (34 men and 46 women) from the Silesian University Hospital, Silesia, Poland, who were between the ages of 12 to 76 and had undergone CT angiography of the circle of Willis. With the use of Gradual Angiographic Image Data Analyser software and double shuttled glasses, CT files were reconstructed. In addition, 80 renal arteries (RAs) from spontaneously aborted foetuses ranging in age from 14 to 30 weeks (24 male and 16 female) were injected with latex and also included in the study. Digital images of the RAs were taken using a Camedia 4040 camera and analysed using original analysis software. A novel formula entitled the Vascular Asymmetry Coefficient (VAC) was derived for this purpose and displays the differences between the mean diameters of blood vessel segments expressed as a percentage of the wider vessel with respect to the major diameter. The asymmetrical classification for a vascular segment of a vessel is given when the difference between the mean diameters of the vascular segment, as represented by the wider vessel, is greater than VAC > 10%. The hypoplastic classification is reserved for blood vessels where the difference between the diameter of the two segments is expressed as a percentage of the wider vessels and is greater than VAC > 40%. While there have been inconsistent and arbitrary classifications for the qualitative criteria of blood vessels, this newly presented algorithm can be used as a standardised tool and has a considerable range of uses, particularly when comparing blood vessel symmetry, asymmetry and hypoplasia prior to bifurcation, and unification.

Key words: symmetry, asymmetry, hypoplasia, blood vessels

INTRODUCTION

In recent years great progress has been made in the field of morphological science with regard to the different procedures used and applied within diagnostic and surgical medicine. This requires objectivity and greater precision in anatomical and comparative measurements. The current standard diagnostic methods used in routine examinations are computed tomography (CT) angiography, magnetic resonance (MR) imaging and ultrasonographic (USG) Doppler studies, as well as other interactive procedures for the visualisation of blood vessels [4, 5, 8, 11, 16, 27, 30, 31].

The advent of faster computers, the higher resolution of digital images and the greater sophistication

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of diagnostic techniques have created a need for new methods of analysing digital images [3, 5, 6, 11, 28]. These new methodologies focus on the quantitative and the qualitative descriptions of blood vessels.

There are numerous varying descriptions of the parameters of the blood vessels, yet researchers are still searching for new parameters to describe vascular structures and the morphology of structures in three-dimensional spaces. The complexity of the problem lies not so much in the expression of parameters such as diameter, length, and volume as in how to compare and interpret these vascular structures using quantitative and qualitative criteria.

Many authors have customarily construed the data subjectively and have not made a concerted effort to use any system of evaluation [1, 7, 24]. This potential error could occur as a result of investigators not fully detailing the methods involved in obtaining quantitative and qualitative values for descriptions of the blood vessels. One of the main issues of concern is that researchers will often not give a through explanation of how they have calculated the symmetry, asymmetry and hypoplasia of blood vessels [7, 19, 22, 24, 29].

Previous reports regarding the various configurations of the circle of Willis (CW) have used 3 main categories of the symmetry, asymmetry and hypoplasia of the segments of CW. For example Krabbe-Hartkamp et al. [11] and Milenkovič et al. [13] used the terms "symmetry", "asymmetry" and "hypoplasia" but failed to give a detailed description of the criteria they were employing.

The symmetry criteria for the segments of the vessels are usually derived from the mean diameter or, in some instances, from other parameters indicated by the authors such as length [1, 2, 9, 21]. These parameters are often based on subjective criteria rather than on a useful quantitative or qualitative evaluation of the blood vessels. It is often the case that the same criteria are used for different population samples, for example foetuses and adults. In some instances they have been used indiscriminately for the measurement of factors that are anatomically distinct, such as the external and internal diameters of blood vessels [1, 2, 24].

The current lack of guidelines calls for detailed and precise procedures to be drawn up. This paper presents a new method for categorising segments of blood vessels as symmetrical, asymmetrical, and hypoplastic using an originally derived formula. The configuration of blood vessels obtained by this method, in contrast to that of other studies, enables an objective assessment to be made.

MATERIAL AND METHODS

A morphometric analysis of blood vessels was made with respect to the brain base arteries of 80 individuals (34 men and 46 women), who ranged in age from 12 to 76 years. The patients were scheduled for imaging of the brain base arteries at the Silesian University Hospital from 2003 to 2005 in connection with various suspected medical conditions and were retrospectively recruited into the study of CW. The CT angiography files were obtained from the patients.

For the examination of the brain base arteries 16-row helical CT scans Mx Twin (Picker/Marconi) with 1024 channels were used. The scanning parameters for helical CT included 120 kV, 241 mA, with a field of view of 12.5 cm, slice thickness of 1.3 mm and slice increment of 0.5 mm. The total scanning time was 32.1 seconds and the scanning time for one full rotation was 1 second. The dynamic focal spot with a 512 × 512 matrix was acquired with a collimation of 1 mm.

Non-ionic contrast material (Omnipaque 350, Amersham) was infused using the MEDRAD Vistron CT semiautomatic injection system into the median cubital vein (80–100 ml at a rate of 3.5–4.5 ml/sec). The scanning process was started after a 16–22 second delay, the length of the delay being dependent on the age of the patient.

The reconstruction of the CT angiography files was performed on institutional Gradual Angiographic Image Data Analyzer (GAIDA) software, which conducted an anatomical and morphometric study of the CW with an interactive post-processing three-dimensional volume-rendering algorithm. All digital files were transferred to a PC equipped with a Core2 Duo E6600 2.80 GHz processor. After automatic segmentation and skeletonisation procedures the segments of CW were obtained and carefully analysed using double shuttle glasses. The arterial segments of CW were measured according to the interactive three-dimensional stereoscopic visualisation technique.

The measurements of the diameter, length and volume of the arterial segments were made after semiautomatic detection. The smallest diameter measured after visualisation of the vascular segment was 0.4 mm. The precommunicating segments of the main trunks of the anterior cerebral artery (ACA), posterior cerebral artery (PCA) and M1 segment of

middle cerebral artery (MCA) were analysed with the use of the vascular asymmetry coefficient formula according to the symmetry, asymmetry and hypoplasia of the segments of CW.

Additionally, 80 latex-injected renal arteries (RAs) were included in the study for more general analysis. The arteries were dissected from 40 spontaneously aborted human foetuses ranging in age from 14 to 30 weeks of gestation (40 left and 40 right RAs, 24 male and 16 female). The abdominal aorta was cannulated with a mixture of 30% suspension latex LBS 3060 and detergent using an automated syringe with a pressure of 5 kPa (37.5 mm Hg) to 20 kPa (150 mm Hg) that infused the arteries of the foetuses. The injection was stopped after cutaneous branches of the superficial temporal artery were filled with latex. The foetuses were then placed in 4% formalin solution, and subsequently the latex was polymerised. Further dissection was conducted to reveal the RAs.

Digital images of RAs were made *in situ* (filled artery with the wall) using a Camedia 4040 camera under the control of analySIS software (Olympus). The digital images were used for the measurement of the RAs (2048 × 1536, 4.1 MPX, BMP). Each of the images was taken while the RA was arranged perpendicular to the longitudinal axis of the lens and were analysed for the diameter, length, and volume of RA by the ANGIOANALYSER 06 software. This program uses multiple pixilation points in order to find the curves of objects analysed (Bezier's curves) to accumulate the measurements used on two-dimensional images.

RESULTS

For the unique morphological and morphometric description of symmetry, asymmetry and hypoplasia of the vascular segments a new formula entitled the Vascular Asymmetry Coefficient (VAC) was derived for this study. The VAC displays the differences between the mean diameter (D) of the blood vessel segments expressed as a percentage of the wider vessel with regard to the major diameter.

If $DVS_L > DVS_R$, the formula for *VAC* is:

$$VAC = \left(1 - \frac{DVS_R}{DVS_L}\right)100\%$$

Table 1. The symmetry, asymmetry and hypoplasia of the precommunicating segment of the anterior cerebral artery (A1), proximal segment of the middle cerebral artery (M1) and precommunicating segment of the posterior cerebral artery (P1) and the renal arteries (RA)

	Symmetry	Asymmetry	Hypoplasia
A1 (n = 80)	57.5%	41.3%	1.2%
M1 (n = 80)	81.3%	18.7%	0%
P1 (n = 80)	32.5%	58.8%	8.7%
RA (n = 40)	60%	35%	2%

and if $DVS_R > DVS_L$, the formula for *VAC* is:

$$VAC = \left(1 - \frac{DVS_L}{DVS_R}\right)100\%$$

where: *VAC* is the coefficient as a percentage of the asymmetry of the vascular segment; DVS_L is the mean diameter of the left vascular segment; DVS_R is the mean diameter of the right vascular segment.

The following criteria for symmetry have been proposed:

— $VAC \leq 10\%$ — the blood vessel is classified as symmetrical;
— $VAC > 10\%$ and $\leq 40\%$ — the blood vessel is classified as asymmetrical;
— $VAC < 40\%$ — the blood vessel is classified as hypoplastic.

In order to determine the requirements for the use of VAC formula it would be helpful to perform the following types of comparison (Table 1).

— precommunicating A1, M1 and P1 segments of the anterior, middle and posterior cerebral arteries;
— bilateral, e.g. right and left RAs (Fig. 1).

Furthermore VAC formula might be used to carry out additional types of comparison:

— bifurcational, e.g. the common iliac arteries branching off the aorta (Fig. 2);
— fusional, e.g. right and left vertebral artery (Fig. 3);
— tributarial, e.g. right and left common iliac vein.

The greatest advantage of using VAC is that it is not only useful for quantitative vascular measurements, such as diameter, but can also provide a through qualitative classification of blood vessels, such as the degree of symmetry.

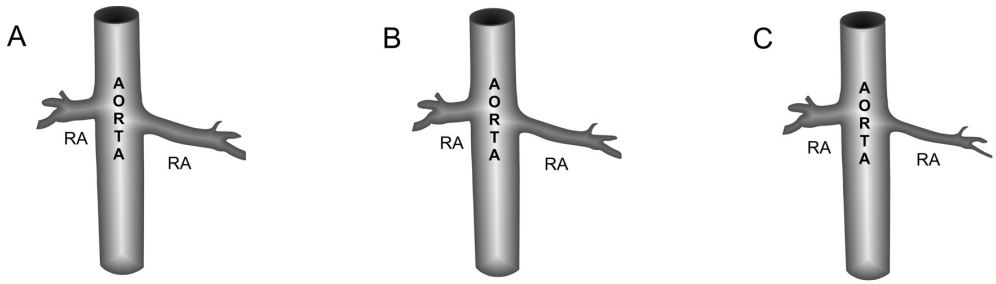

Figure 1. Diagram of the bilateral type of arterial symmetry (**A**), asymmetry (**B**) and hypoplasia (**C**); RA — renal artery.

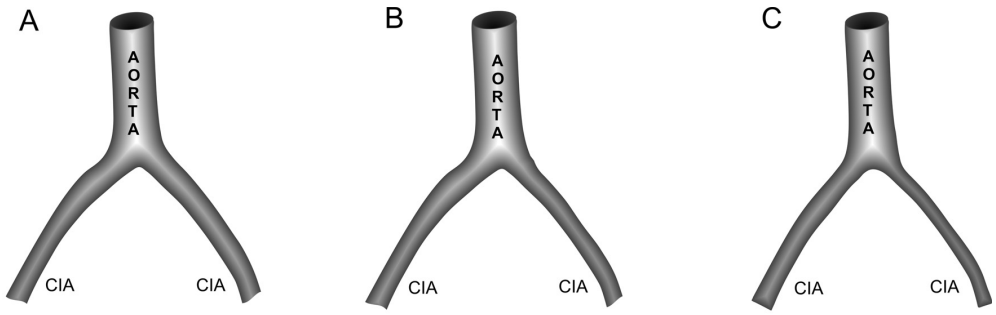

Figure 2. Diagram of the bifurcational type of arterial symmetry (**A**), asymmetry (**B**) and hypoplasia (**C**); CIA — common iliac artery.

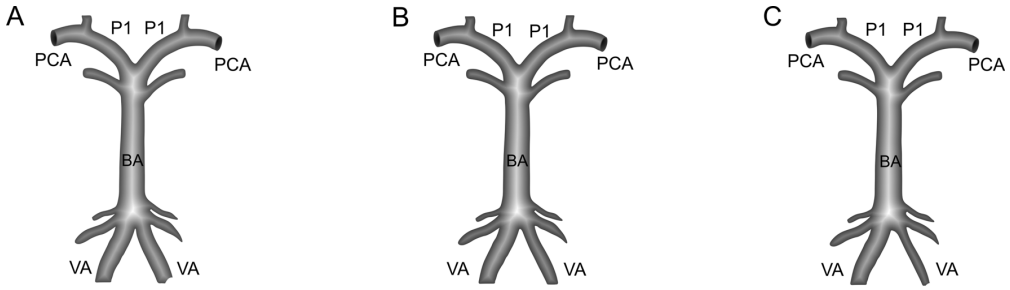

Figure 3. Diagram of the segmental (P1) and fusional (VA) type of arterial symmetry (**A**), asymmetry (**B**) and hypoplasia (**C**); P1 — pre-communicating segment of posterior cerebral artery, PCA — posterior cerebral artery, VA — vertebral artery, BA — basilar artery.

DISCUSSION

Blood vessel diameter is the most frequent and accurate parameter analysed by different authors for the purpose of comparing vascular variations [3, 9, 11, 12, 13, 19, 25]. However, diameter sizes may be dependant on the pressure which is exerted by a plastic mass such as latex while the blood vessel is being injected, the technique of filling the vessels, the methods of preservation and the generalised method used for calculations. Accordingly, there may be many inaccuracies when comparisons are made between the different published data [11, 21, 24].

For this reason there have been many arbitrary classifications and inconsistencies between published studies. It is with this aim of greater clarification and uniformity that the novel qualitative criteria of blood vessel symmetry, asymmetry and hypoplasia, defined as the VAC, has been proposed.

The evaluation of the diameter and the length or volume from different studies might be achieved by

using the concise VAC formula. However, various methods have been applied during such investigations, including post-mortem studies, digital image analysis, USG, CT angiography, digital subtraction angiography and MR angiography. All these methods made good use of VAC formula. Furthermore, this formula could be used for comparing foetal, newborn and adult blood vessel parameters. It may be an ideal tool for improving quality and objectivity during morphometric evaluation.

Kalsho et al. [9], who primarily focused on the coronary blood vessels and their bifurcations, analysed the asymmetry of the vessels using the diameter and other parameters, such as the length, of their segments. They gave attention to the essential characteristics of vascular asymmetry at a bifurcation point in the blood flow [9].

The proposed VAC formula can be used to compare a blood vessel's symmetry, asymmetry or hypoplasia after its bifurcation, for example for the common iliac arteries, external and internal iliac arteries, external and internal carotid arteries, ACAs, MCAs and others. Comparisons can also be made before the vessels join, as in the case of the vertebral arteries. It can also be helpful to compare right and left vessels that possess the same name, for example the right and left common iliac arteries, ACAs or RAs. The algorithm of VAC can be applied in studies of all blood vessels, including those of the brain, coronary and peripheral systems, as well as the arteries and veins. It is also possible to compare vascular segments and to make accurate evaluations of their symmetry, asymmetry or hypoplasia.

Attempts to compare data for various vascular segments published by different authors have encountered difficulties in interpretation, and at times it has been impossible even to compare the data owing to the inconsistencies of the methods applied and the specimens selected [1, 11, 17, 23, 24].

Many questions have been raised in previous studies with respect to the research of different authors regarding the diameter of a certain vascular segment. When a segment has been slightly larger on the left side than on the right it has been questioned whether it should be classified as asymmetrical or symmetrical. An objective answer to this question has been elusive [1, 7, 19, 23, 24]. Often, authors have used terms such as "normal vessel" or "normal CW" [1, 29]. It is unclear what exactly is meant by such terminology and the assertion of normality. The concept of "normal" with regard to blood vessels could encompass the symmetrically paired vessels of CW or might be the complete CW with all the arterial segments clearly visible. The difficulty is that the concept of "normal" is very much a subjective term and is ambiguous in nature. A further example is the work of Pallie et al. [20], who defined the "normal" CW as symmetrical and complete. Some authors have used the term "normal vessel" for a vessel with a diameter of more than 1 mm set as the lower limit [2, 23]. According to Kamath [10], vessels with a diameter of less than 1 mm, such as the ACA, or 0.5 mm for the communicating arteries, are both defined as "abnormal blood vessels". This begs the question as to whether what is defined as an "abnormal vessel" could also be identified as hypoplastic?

Furthermore, in previous publications no clear rule has emerged governing the classification of the hypoplastic vascular segments. Until recently a hypoplastic segment was described as a segment with a very small diameter, according to arbitrary interpretations. No clear definition was given of what was meant by "very small diameters". The criteria used to make such measurements and conduct the analysis have often been inadequately explained [16, 23, 29]. As for the hypoplastic criteria, some authors have proposed that the absolute diameter of blood vessels be taken into account but have failed to state whether the external or internal diameter should be used for the assessment [2]. This common problem is eliminated by VAC owing to the fact that the diameters of 2 arteries are compared in proportion to one another and in terms of the absolute measurement of diameter. The internal and external measurements of blood vessel diameter thus become obsolete.

Some researchers have accepted arteries with diameter sizes smaller than 1 mm as hypoplastic [2, 10]. This is not conducive to objective methodology, although sometimes the internal or even the external diameter of a blood vessel have been analysed and compared in similar terms. It should be noted that a blood vessel's diameter is dependant on several factors, including age, sex, race and genetic differentiators. Thus a 1 mm diameter cannot be generalised to all population samples.

Furthermore, Krabbe-Hartkamp et al. [11] stated that the hypoplastic classification applies to a blood vessel with a diameter of less than 0.8 mm with the use of MR imaging and less than 0.6 mm using anatomical dissection for autopsy studies [11]. Milenkovič et al. [13], whose studies where conducted on foetal arteries, concluded that a diameter of less than 0.3 mm for an A1 segment of the ACA and less than

0.2 mm for a P1 segment of the PCA qualified for classification as hypoplastic [13].

Perlmutter et al. [21] analysed the brain base arteries in adults and suggested that all segments with a diameter less than 1.5 mm should be classified as hypoplastic.

Riggs et al. [23] defined the hypoplastic CW as a vessel with just one hypoplastic segment (A1 or P1) or as artery with several hypoplastic segments at the same time.

The problems faced by researchers in analysing the data has forced some of them to put into place a new measurement system and to form an objective criterion for the morphometric evaluation of the vascular segments as a corrected or a rectified circumference [14, 15, 18] or even as a weighted mean diameter [6]. Only Kalsho et al. [9] have proposed a mathematical algorithm for the evaluation of the vessel parameters, with special attention given to the blood flow. No other previous authors constructed a simple objective system for evaluating the investigations of different researchers. Any system devised should enable a comparison to be made of the quantitative and qualitative data. In a situation where there is no clear, explicit definition of the criteria of symmetry, asymmetry and hypoplasia of the vessels, it is not possible to compare the data from different studies. It is important to note that each of the research evaluations ultimately produced different results. In most of these studies the reason was the lack of standards used in description of the vascular segments.

The purpose of proposing the VAC formula as a given percentage is that it allows clear, straightforward morphometric criteria to be used, which can make it possible to define the type of blood vessel and also to standardise the methods of different studies. In addition, a novel definition of symmetry, asymmetry and hypoplasia has been proposed with the vascular segments classified according to the VAC formula.

In order to conform to the new morphometric rules, an asymmetric vascular segment was recognised when the difference between the mean diameters of the vascular segment represented by the wider vessel was greater than VAC > 10%.

The hypoplastic classification applies to a vessel where the difference between the diameter of the two segments, expressed as a percentage of the wider vessel, is greater than VAC > 40%.

Knowledge of hypoplastic vessels is of great help and importance when the etiology of aneurysms and other vascular malformations is considered. The anatomical differences and vascular variations may be the cause of clots, aneurysms and a variety of other neurological problems [16, 26].

The VAC coefficient may be applied to the analysis of the blood vessels of foetuses, neonates, children and adults. The algorithm may be relevant when comparing the diameters of vessels after their bifurcation or before fusion. There are no limitations to the application of the VAC formula. It may be used in investigations based on post-mortem studies, angiography, CTA or MRA.

The VAC formula can be a powerful tool in describing the morphometry of the vessels and in improving standardisation and reproducibility. However, the simple algorithm, in which current and published data have been applied, may also be used as a clinically useful tool. The algorithm is necessary for blood flow simulation and for the planning of vascular repair procedures. It can provide radiologists and vascular surgeons with better quantitative estimates, which may be used to measure the parameters and the blood flow before and after endovascular or extravascular procedures. It may also help in differentiating asymmetry or hypoplasia from the pathological narrowing of vessels resulting from atherosclerosis or radiotherapy.

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