"OVIDIUS" UNIVERSITY OF CONSTANȚA
DOCTORAL SCHOOL OF MEDICINE
THE FIELD OF MEDICINE

THESIS
SUMMARY

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PhD student:
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CONSTANȚA
2021

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INTERNAL CAROTID ARTERY MORPHOPATHOLOGY SUMMARY

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LIST OF PUBLICATIONS

Articles published in journals:

1. Baz RA, Scheau C, Sârbu N, Costea DO, Dijmărescu A, Bordei P. Carotid paragangliomas: case report and imaging review. Folia Morphol (Warsz). 2021; 80 (3): 699-706. doi: 10.5603 / FM.a2020.0078. Epub 2020 Jul 25. PMID: 32710793.
2. Baz RA, Scheau C, Niscoveanu C, Bordei P. Morphometry of the Entire Internal Carotid Artery on CT Angiography. Medicine. 2021; 57 (8): 832.
3. Baz RA, Apostol E, Niscoveanu C, Bordei P, Munteanu O. Common carotid artery bifurcation geometry on CT angiography. Romanian Journal of Functional and Clinical Anatomy, Macro- and Microscopic and Anthropology, 2021, vol XX, no. 3: 164-167.

Articles accepted for publication:

1. Baz RA, Apostol E, Niscoveanu C, Bordei P. Course variations of the cervical internal carotid artery - article approved for publication in the Romanian Journal of Functional and Clinical Anatomy, Macro- and Microscopic and Anthropology, 2021, vol XX, no . 4.

Papers presented at scientific events:

1. Baz RA, Baz R, Piti M, Apostol S, Sachoulidou A. Morphometric relations between the branches of the aortic arch. XXth National Congress of the Romanian Society of Anatomy, May 16-19, 2019, Constanţa, Romania.

TABLE OF CONTENTS

Working hypothesis and general objectives

The main vessel that brings oxygenated blood to the brain is the internal carotid artery (ICA). Any type of damage to this artery can cause irreparable changes to the central nervous system, and the best way to combat pathology in the carotid sphere remains prevention. A good knowledge of both the normal carotid and the pathology of the vessel is imperative for any doctor. The internal carotid vascular system highlights a multitude of anatomical variants regarding the origin, trajectory and ratios, morphometry (diameter, length), as well as the distribution of its collateral and terminal branches. Because a correct and detailed signaling of anatomical variations can influence the therapeutic attitude towards the patient, a good part of the pathologies affecting ICA can be better and easier to manage, thus avoiding unwanted consequences.

ICA pathology also shows great variability, ranging from the most common condition, namely atherosclerotic disease, to extremely rare pathologies, such as carotid axis tumors. A wide range of imaging changes can be seen in the case of internal carotid pathologies, but with an early signaling of often ignored changes, the consequences may not determine the sequelae that affect patients' quality of life or lead to disabling impairment.

The exploration of internal carotid vessels has evolved in recent years, so that, from simple angiography by direct puncture of the artery, angiography by magnetic resonance can be currently performed without contrast, a type of examination that highlights the circulating flow. Computed tomography angiography (CTA) remains today the most used method of investigation of carotid arteries, combining excellent sensitivity and specificity in the evaluation of vascular changes, a good quality / price ratio and wide availability, but having as disadvantages the use of ionizing rays and iodinated contrast.

The general premise that initially formed the basis of the study was that computed tomography imaging currently plays a key role in diagnosing and monitoring patients with atherosclerotic carotid disease, as the detection and classification of ICA lesions can be easily done through CTA. In addition, early detection of fine changes in vascular structure is an effective method for preventing the progression of carotid atherosclerotic pathology. CT imaging is the most widely used way to assess the extent of the disease and the response to therapy, while allowing the detection of alarm signs or complications.

This study is based on CTA, performed on patients at the indication of the attending physician, in cases with history of cerebral ischemic phenomena, in cases selected by clinicians in syncope,

vertigo, headache, carotid murmurs or other conditions especially in the neurological sphere, respectively in case of direct addressing of the patient with the procedure on request.

The aim of this paper is to present both the normal and pathological configuration of ICA, as well as to determine geometric differences between normal and pathological artery, thus having the opportunity to signal potential risk factors related to anatomical parameters of the artery. The purpose of these comparisons is to determine discrete variations in the morphology and geometry of the disease-free vessel, also visualized in patients with present vascular lesions, so that, by carefully evaluating anatomical indices, thus in the near future a much stricter monitoring of the vessel could be performed and possibly an early therapeutic attitude for patients at risk for carotid atherosclerotic disease

The general objectives of the thesis were the following:

- presentation and illustration of CT aspects of normal ICA;
- establishing the semiological elements of CT for ICA with associated pathology;
- measurement of morphometric and geometric indices of ICA, both on normal vessels and on those with associated lesions;
- corroboration of the data obtained in order to identify anatomical risk factors;
- elaboration and recommendation of a new type of result (interpretation) of CT angiographies that would systematize anatomical variations with clinical and / or surgical significance.

Material and methods

We performed a prospective descriptive observational study, performed on a number of 314 arteries analyzed on CTA angiographies centered on the carotid axes, performed within the Emergency County Clinical Hospital "Sf. Apostol Andrei" Constanța, during 01.10.2017 - 01.10.2019.

The study group consists of 162 adult patients, included in the personal database regardless of gender, origin, race, profession or religious orientation.The exclusion criteria from the study are the following:

- patients under 18 years of age;
- patients with low quality examinations, either because of the inability to maintain the apnea required for scanning or movement, or because of metal artifacts generated by various accessories / implants that could impair measurements;
- examinations in cases of polytrauma with carotid involvement.

The effective working methodology included the following steps:

- identification of the examinations according to the study, according to the inclusion and exclusion criteria mentioned;

- obtaining informed consent from the patient and inclusion in the study group;

- analysis of images and recording of information obtained from measurements in the database;

- statistical interpretation of data obtained from measurements.

Examination protocol:

Initially, the patient is prepared, which consists of:

- obtaining informed consent and signaling possible contraindications to contrast administration, including a known history of allergies;
- the 18-20 G branula is positioned and / or checked.

Patient positioning and acquisition:

- in supine position, having the cranial extremity in gantry; the front and profile topogram is made;
- the area of interest from the aortic arch to the base of the skull is covered;
- the initial locator is obtained at the level of the carina with a region of interest (ROI) set on the path of the aortic arch;
- the injection of the contrast medium is triggered;
- the examination is initiated automatically when the aorta is opacified with sufficient contrast medium;
- when a concentration of at least 120 Hounsfield Units (UH) is detected in the aortic arch by the "bolus tracking" method, the scan is triggered;
- the carotid axes are scanned in arterial time in caudo-cranial direction.

The CT acquisitions were made on two distinct installations, namely LightSpeed VCT64 Slice CT General Electric (USA, Chicago, Illinois), respectively Somatom Emotion Siemens 16 slice (Germany, Forchheim). Basic image processing is performed on a workstation produced by General Electric (Advantage Workstation) and uses specific angiographic software (eg VesselIQ Xpress). We made reconstructions from the source images such as:

• three-dimensional MPR (multiplanar reformation);
• curvilinear reformations;
• MIP (maximum intensity projection) images;
• VRT analysis (volume rendering technique - fig.1).

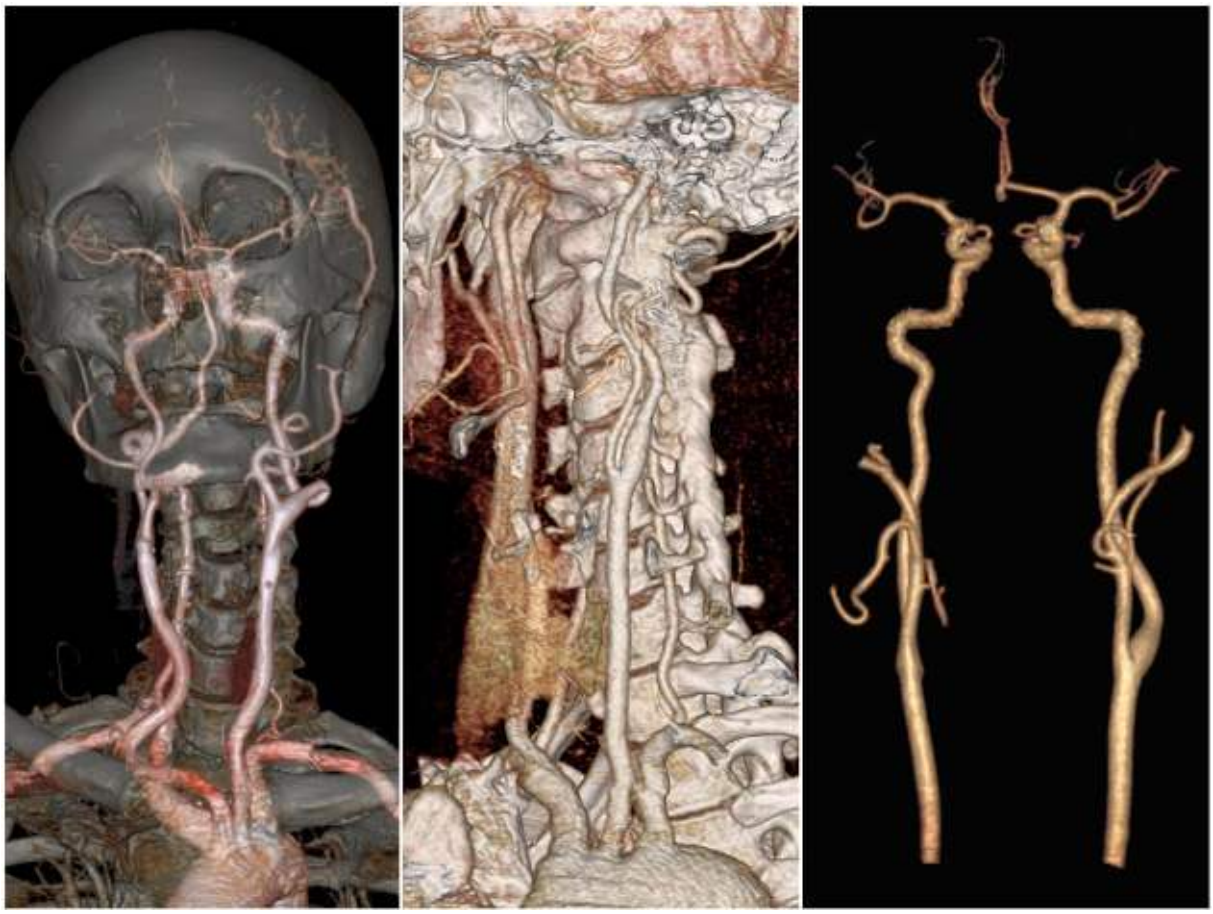


Fig. 1. Various types of MIP reconstructions.

We divided the patients into two groups: a group with disease-free ICA and a group with ICA affected by carotid pathology. In the first part of the present study, we evaluated the morphometric and geometric characteristics on a group of 152 normal ICA, without detectable CT atherosclerotic lesion.

Target measurements

Vascular caliberswere analyzed bilaterally in carotid vessels. The diameter was initially calculated semi-automatically in all vessels and the values were obtained at the level of the regions of interest. The diameter was then calculated based on the axial plane source images by manual measurements. Measurements for CCA, ICA and external carotid artery (ECA) morphometry were performed as follows:

I. CCA: maximum diameter before bifurcation;

II. ECA: maximum immediate cranial diameter of the CCAbifurcation;

III. ICA:

1. the diameter at the origin, at the most dilated point of the carotid sinus;
2. height (length) of the carotid sinus;
3. diameter after physiological dilation of the ICA root;
4. the mid-carotid diameter, measured in the middle of the ICA distance in its extracranial portion;

5. diameter at the base of the skull (preforaminal);
6. the diameter at the level of the petrous segment (C2);
7. the diameter of the lacerum segment (C3);
8. diameter at the level of the cavernous segment (C4);
9. diameter at the level of the clinoid segment (C5);
10. diameter at the level of the ophthalmic segment (C6);
11. the diameter at the level of the communicating segment (C7).

Also we measured the ICA length in the cervical and intracranial portion, the level of its origin depending on the cervical vertebrae, as well as the angles between ICA and ECA (bifurcation angle), respectively between ICA and CCA. We also appreciated the ICA course in the cervical portion, determining the type and frequency of variations encountered. We measured by the same methods the dimensions of the ophthalmic artery (OA).

The group studied in the second part of the thesis consists of 162 ICA, this time either with atherosclerotic lesion present, or with tomodensitometric changes suggestive for a traumatic / inflammatory / tumor pathology. The main objective of these CT examinations, according to the request of the attending physicians, was to evaluate the carotid lesions and the patency of the vessels, so we performed a detailed analysis of the carotid pathologies encountered in order to develop an appropriate imaging result.

Atherosclerotic stenoses were classified NASCET-type according to their severity, being grouped as follows:

- mild stenoses, with obstructed lumen <50%;
- moderate stenosis, with obstructed lumen> 50% and <70%;
- severe stenosis, with obstructed lumen> 70% and <90%;
- critical stenoses, with obstructed lumen> 90%.

The type of stenoses was classified according to the composition of the atherosclerotic plaque according to UH as follows:

- soft plaque (with lipid content) at densities < 60 UH;
- hard plaque (calcified) at densities > 130 UH;
- mixed plaque, at values > 60 and <130 UH.

After evaluating the pathological changes encountered in ICA, we determined the anatomical indices used in the group of normal arteries, namely the origin of the cervical vertebrae, length, trajectory variants, bifurcation angle and, respectively, the origin angle of ICA.

Synthesis of chapters

The doctoral thesis consists of two parts - "Current state of knowledge" and "Personal contribution". The first part of the thesis, the general part, presents a synthesis of the information in the literature regarding ICA. In the general part data about the anatomy of ICA is presented, as described by classical and contemporary authors; citing both recent works using new imaging methods as well as reference works in the field, performed on corpses or classical angiographies, we detailed the morphometric analyzes of the vessel, reports from well-known writings on the diameter, length and angles of ICA.

Personal research refers both to the determination of the morphological characteristics of the intact ICA and to the determination of the morphological characteristics of the arteries with pathology. Initially, we determined the morphometric indices of normal ICA, in order to subsequently measure a part of these parameters (which are suitable for measurements) within the group of patients with pathological ICA.

In patients with pathological ICA I noticed peculiarities in carotid atherosclerotic disease and I presented other pathologies encountered in the institution where I work. The results we obtained were illustrated by personal images, graphs and tables, later marking comparisons with existing data from the literature that we had the opportunity to consult. After obtaining the data, we performed a detailed statistical analysis of the information, determining more or less different values between the sexes, depending on the level of ICA origin, the studied parts (right and left), age groups. We ran the statistical tests in the dedicated Medcalc® software, mainly using basic formulas such as the T test, the Pearson correlation, the ANOVA test, the Chi test.

The purpose of the analysis was to identify normal morphometric indices of ICA in CTA, morphometric indices in pathological ICA and, respectively, highlighting correlations between these two entities that may reveal unfavorable developments in patients at risk of carotid atherosclerotic disease.

Results

In the group of patients with disease-free ICAs we did not observe significant differences between sexes or parts studied in terms of the level of bifurcation of the CCA, finding similar results with the authors of studies focused on the CCA bifurcation level (Table 1).

Table 1. Normal ICA origin level

Authors	Normal ICA level (C3-C4)
Zumre	90%
Anu	90%
Klosek și Rungruang	67%
Ito	57,5%
Personal results	69,73%

Using the methods described above, we measured the angles formed by ICA with ECA, respectively with CCA and we performed correlations depending on the studied part and the sex of the patients, comparing the results with data from the literature (fig. 2). We identified insignificant differences depending on the studied part and depending on the sex in terms of ICA angles (Table 2).

Table 2. ICA angles

	ICA-ECA (°)	**ICA-CCA (°)**
J.B. Thomas	48,5 ± 6,3	
Phan	23,3 ± 14,01	
X. Huang	36 ± 16	144 ± 13
Personal results	41,70±9,94	136,19±15,94

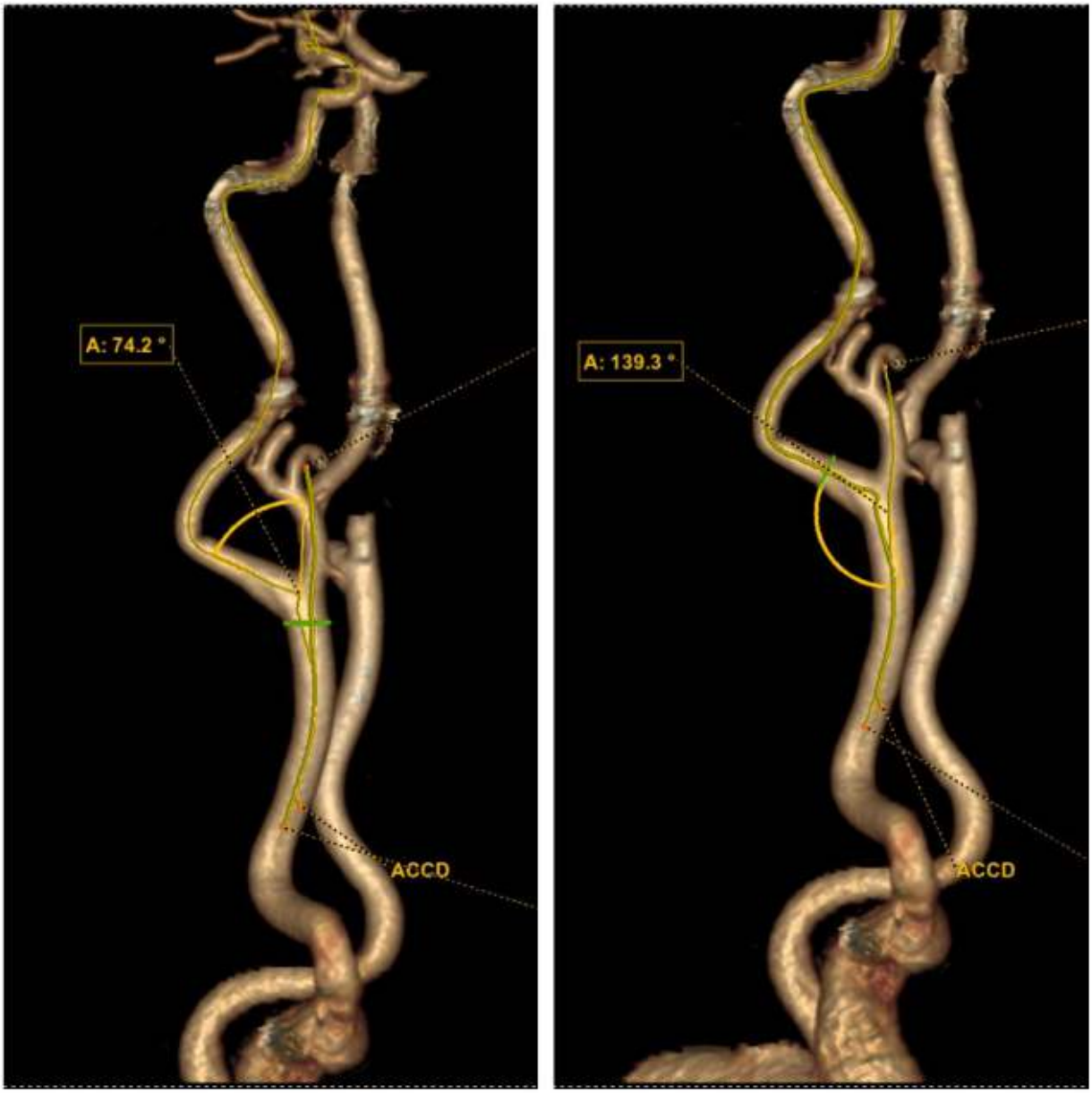
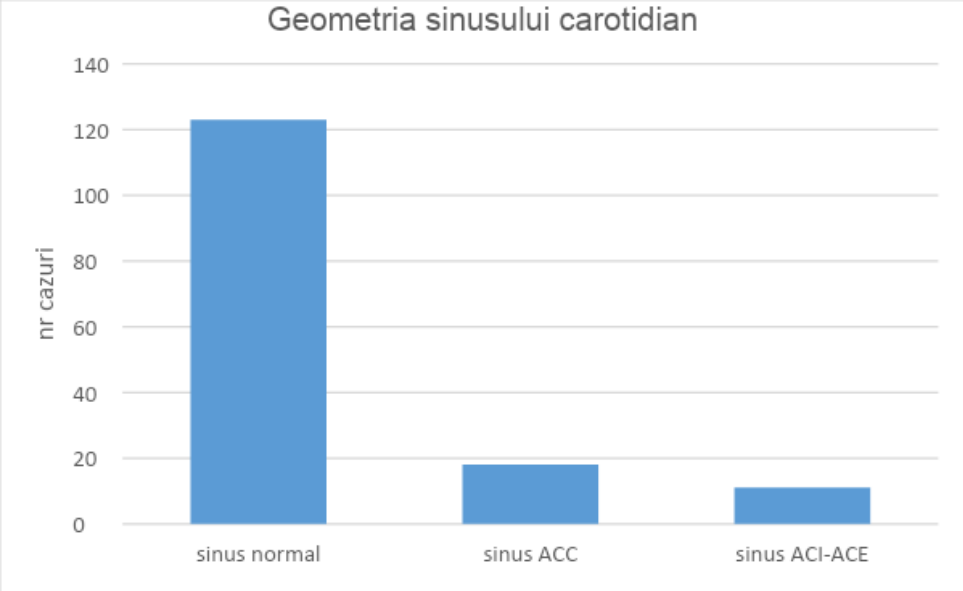


Fig. 2. Increased values of the bifurcation angle (74 °) and low values of the emergency angle (140 °).

At the level of the ICA sinus we determined values similar to those in the literature (table 3), obtaining the average value of 7.6 mm, without differences depending on the studied part. We determined by means of the bidirectional Welch T test significant statistical differences ($p < 0.05$) in terms of sinus diameter according to sex, obtaining values of 7.87 ± 0.96 mm in males, respectively 7.33 ± 0 , 90 mm in females. We found a positive correlation between the age of patients and the size of the sinus region of the ICA (r-0.23, $p = 0.004$), higher diameter values being visualized in older patients. The length of the carotid sinus was on average 9.67 ± 2.12 mm, without statistically significant differences depending on the studied part, but with clear differences depending on sex, in the case of men the sinus being longer ($p = 0.005$).

Table 3. ICA sinus diameter

Authors	ICA sinus region (mm)
Kamina	9
Paturet	9
Goubergrits	7,38
Kamenskiy	7,97
Personal results	7,6±0,97



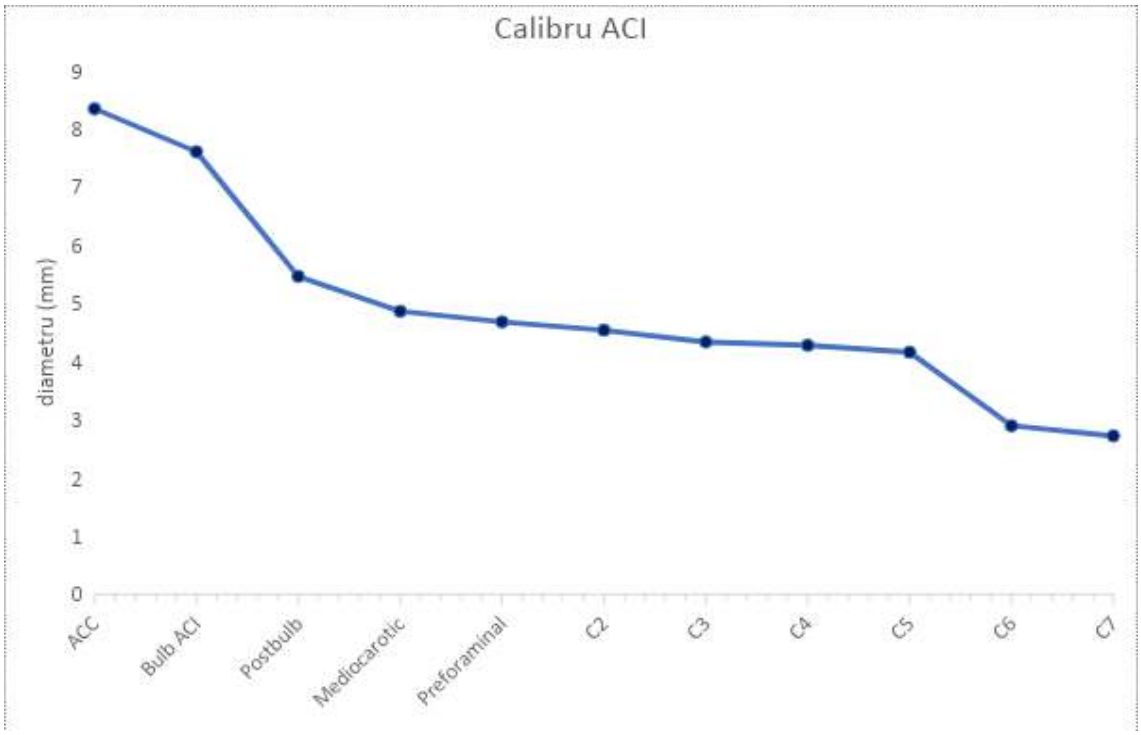
Graph 1. Numerical distribution of carotid sinus orientation variants

Regarding the orientation of the carotid sinus, we demonstrated normal CT appearance visualizing the physiological dilation on both the terminal CCA and the proximal ICA in 81% of cases (n = 123). In 11.84% (n = 18) of cases we noticed that the sinus dilatation does not extend on the terminal branches of CCA, and in 7.23% (n = 11) of cases we showed a proximal vascular dilatation on ICA as well as on ECA.

Measurements of the ICA diameter in both the extracranial portion and the intracranial portion are shown in Table 4, noting that in the extracranial carotid, in addition to determining the carotid sinus (C1a), we also measured the carotid in the middle of its cervical trajectory (C1b) and, respectively, before traversing the carotid canal (C1c). The physiological decalibration of ICA throughout its trajectory is highlighted in graph 2. We established statistically significant differences between the sexes up to and including the C5 level, without highlighting differences depending on the studied part.

Table 4. ICA diameter analysis (mm)

C1a	7,6±0,97
C1b	4,86±0,52
C1c	4,68±0,46
C2	4,53±0,46
C3	4,30±0,42
C4	4,27±0,44
C5	4,15±0,47
C6	2,89±0,39
C7	2,72±0,37



Graph 2. ICA caliber by its segments.

The evaluation of the entire length of the ICA reveals total dimensions of approx. 15 cm, comparative results with both cadaveric and angiographic studies (Table 5) [12, 13]. We did not detect differences depending on the studied part; [13] also finds similar values in the cadaveric study performed, of 14.9 mm on the right side and 14.8 mm on the left side.

Table 5. ICA length

Authors	ICA Length (mm)
Francke	150
Shashikant	148.5
Personal results	155

The interpretation of the course variants of ICA was classified according to the established studies in the literature [14-16]. The interpretation technique and the types of variants of the ICA path encountered in this study group are presented in fig. 3, and in table 6 are presented comparisons with the literature.

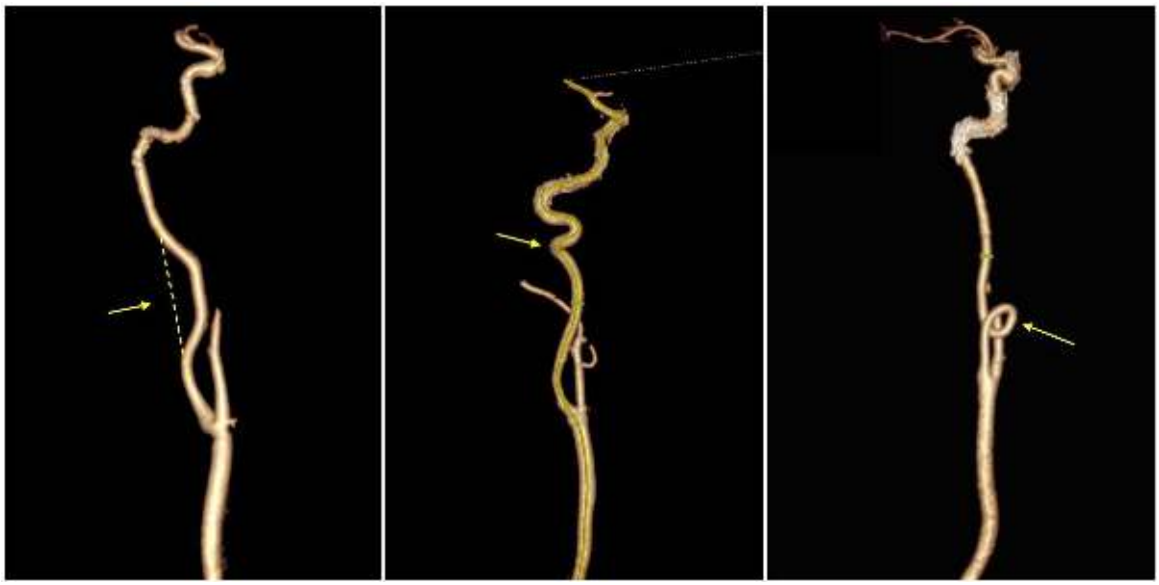


Fig. 3. Carotid variations (arrows): medial elongation (dotted line simulates normal course), kinking and coiling.

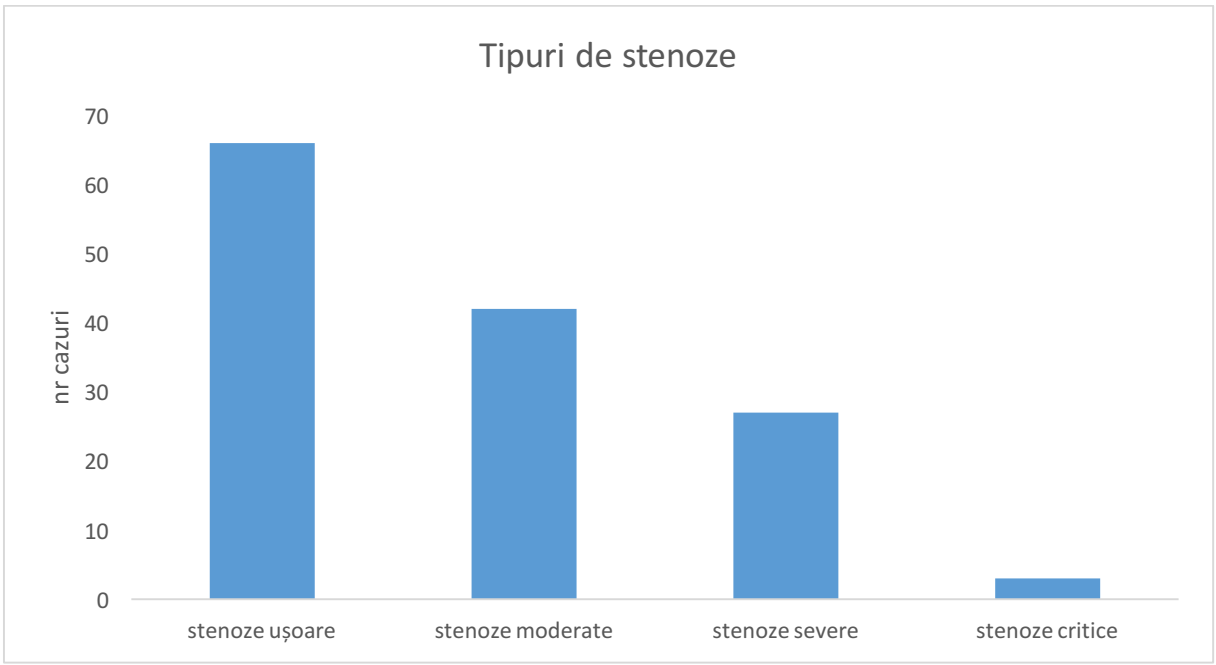
Table 6. ICA course variation

Authors	**Dolicoarteriopathies frequency**		
	General	**Kinking**	**Coiling**
Nagata	85,8%	1%	3%
Pellegrino	26%	14%	2,9%
Dilba	69%	13%	5,5%

Personal results	48%	13%	4%

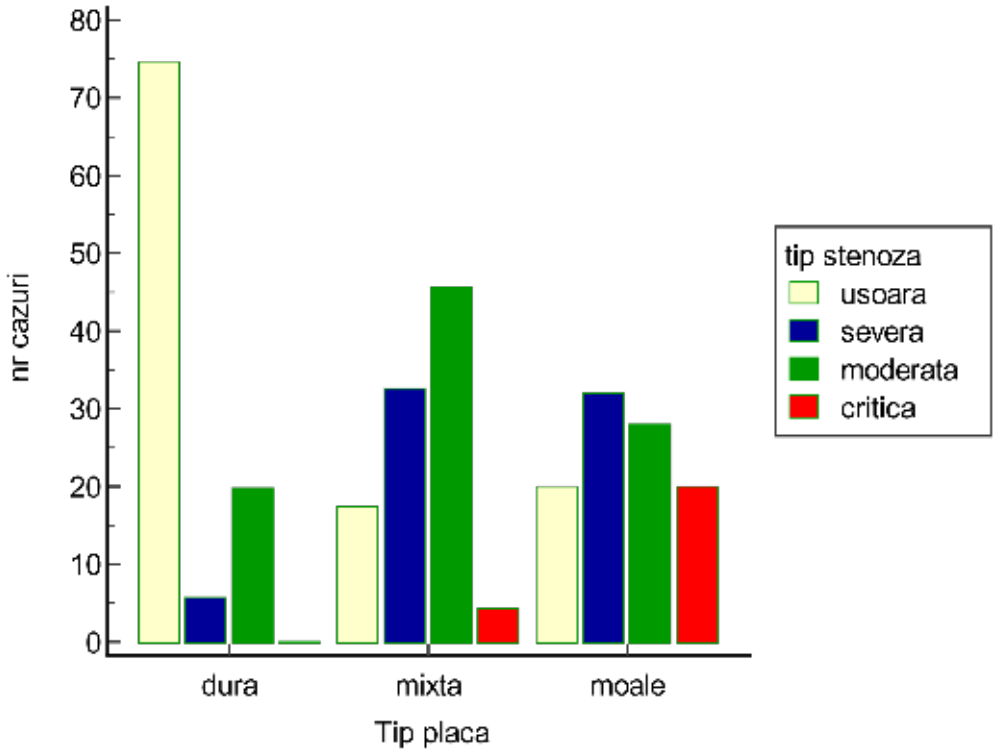
Regarding the course anomalies of the ICA, we did not demonstrate positive correlations between sexes, studied parts or the origin of the vessel, but we demonstrated strong correlations with the length of the vessel ($p < 0.05$), so a more sinuous vessel is usually, longer. Also, through the ANOVA test we demonstrated a positive correlation between the age of the patients and the presence of sinuosities, in older patients these course variants being more frequently encountered.

Atherosclerotic carotid disease is the most common type of lesion with internal carotid localization. Atherosclerotic damage is usually imaged, as an atherosclerotic plaque of varying consistency, most often with calcareous (hard) deposits. Atheroma plaque can be characterized by CT imaging as a function of density, thus dividing into lesion with lipid core (low densities, sometimes negative), fibrous plaque (medium densities) and, respectively, hard plaque (much higher densities). CT angiography determines the local degree of involvement in atherosclerotic stenoses, as well as the type of lesions (graphs 3, 4).



Graph 3. Types of stenoses.

We classified atherosclerotic lesions in our study according to one of the early works on the analysis of atheromatous plaques on CT [20]. The literature claims that non-calcareous plaques more frequently cause both severe stenoses in terms of imaging classification and symptomatic stenoses [21]. In our study, severe stenoses are more commonly associated with mixed or soft atheromatous plaques.



Graph 4. Association of the atherosclerotic plaque type with the degree of carotid stenosis

According to our study, there are no statistically significant differences in the types of atherosclerotic plaques that affect ICA between the sexes, male and female, after applying the Chi test ($p = 0.6$, contingency coefficient of 0.227), hard plaques being the most common, numerically similar. In the group of patients with pathological ICA we also measured ICA angles, carotid length and sinuosity, demonstrating differences similar to the group of patients without stenosis: differences between sexes in terms of lengths, small difference in ICA-CCA angle between sexes, without differences in the studied parts regardless of the selected parameter. Subsequently, we compared these data with the values obtained in the group of patients with disease-free ICA.

There are statistically significant differences (p <0.001) between the bifurcation angle for the group with normal ICA and the bifurcation angle for the group with atherosclerotic ICA, visualizing average differences of approx. 16 degrees between groups.

Table 7. ICA-ECA angle

Authors		**Normal vessel ICA-ECA angle**	**Diseased vessel ICA-ECA angle**
Noh	right	26,89 ± 8,07	34,10 ± 7,88
	left	31,77 ± 13,58	41,81 ± 10,93
Thomas		48,5 ± 6,3	63,6 ± 15,4
Huang		36 ± 16	42 ± 20
Personal results		41,70 ± 9,94	58,15 ± 17,5

We found a similar correlation in the case of the ICA-CCA angle compared to the two groups, obtaining a p value <0.001 in the t test, the origin angles for the group with atherosclerotic disease being smaller (136.19 compared of 145.03 degrees).

We observed a good correlation, with statistical significance (p <0.0001 in the t test), for the total length of the internal carotid in the two groups, observing significantly higher values of ICA length among carotids affected by atherosclerotic disease.

Tabele 8. ICA length

	Normal ICA length	**Diseased ICA length**
Study group	142	142
Mean value	153.3352	168.1317

Course variants are most common among males with associated atherosclerotic pathology, as seen in the following table.

Table 9. Course variations in both groups by sex

	normal ICA		**diseased ICA**	
Gender	F	M	F	M
Normal course	53% (N=39)	47% (N=34)	36% (N=12)	64% (N=21)
Abnormal course	47% (N=37)	53% (N=42)	35% (N=38)	65% (N=71)

The normal, rectilinear trajectory of the ICA is generally found in younger people, data shown in the following table. Pathway variants are often found in people> 60 years of age and are also seen more frequently when there are carotid atherosclerotic changes, as described in studies. [23]

Tabel 10. Course variations in both groups by age

	normal ICA		**diseased ICa**	
Age groups	<60 ani (N=82)	>60 ani (N=70)	<60 ani (N=31)	>60 ani (N=111)
Normal course	60% (N=50)	32% (N=22)	42% (N=13)	18% (N=20)
Abnormal course	40% (N=32)	68% (N=48)	58% (N=18)	82% (N=91)

Other carotid pathologies encountered in the study group outside atherosclerotic disease were rare, considering the inclusion in the study of consecutive pathological arteries, totaling 6.17% of cases of pathological ICA. We detected carotid aneurysms, changes in muscle fibrodysplasia and carotid paragangliomas, presenting typical tomodensitometric aspects.

General conclusions

ICA is an area of interest in modern medicine for many reasons. The diagnosis, prognosis and treatment of carotid pathologies are based on precise anatomical knowledge in this field. The consultation of the specialized literature showed gaps in certain characteristics related to the knowledge of ICA and, in particular, on the population group with normal arteries, without detectable pathological changes. The aim of the study was to determine the anatomical, geometric and morphometric variations of ICA, so that later we can compare certain parameters with the results of the group of pathological arteries. We observed that the patients included in our study group presented certain variations of ICA that correlated with what is reported in the literature [5, 24]. We also found changes in anatomical indices in patients with atherosclerotic ICA, compared to the group of patients without carotid pathology.

This study illustrated morphometric indices (diameter, length) of the normal carotid artery, performing multiple measurements for a better understanding of vascular anatomy. There was an obvious difference between the vascular diameters of the male subjects compared to the female population in our group, the men presenting higher values from the origin of ICA. Similar differences, statistically significant, were detected in the case of carotid artery length.

Age also influenced morphometric indices, demonstrating higher values of CCA and ICA caliber, respectively of ICA length, at older ages, similar to studies published in the international literature [11, 25].

The carotid sinus was highlighted in a normal configuration in only 81% of cases, the rest being considered anatomical variants, a report similar to another recently published study [26]. The anatomical features and variations of the carotid sinus are current topics of discussion in the clinical and surgical field, both in terms of carotid sinus syndrome and incomplete sinus excision in the case of endarterectomies. [27-29]

In the group of patients with diseased carotid arteries we found differences between the angles studied as follows: the bifurcation angle was 58.15 degrees (compared to 41.70 in normal ICA) and the origin angle was 136.19 degrees (compared to 145.22). Such differences are presented in the literature [5, 7], so that the angles formed by the internal carotid artery with either ECA or CCA could be used as a method of screening patients at risk for atherosclerotic carotid disease. We also observed discrete longer ICA lengths (by 14.8 mm) in the group of patients with pathological arteries, this aspect showing statistical significance in all measurements on ICA length (extracranial, intracranial, total).

The course variations of the extracranial internal carotid were more numerous in the group of patients with carotid atherosclerosis, being noted in 73% of cases, as opposed to 52% in the group of patients with normal ICA. The ratio of the types of variants remained similar to the group with normal ICA, the elongations being the most frequent, followed by angulations and vascular loops. We obtained a positive correlation between the age of the patients and the presence of course variants, but we did not demonstrate an influence of the height of the carotid bifurcation on the presence of sinuosities, contrary to a report in the literature. [30]

Through the present study we demonstrated normal and pathological aspects of ICA, achieving statistically significant correlations between some of the anatomical parameters evaluated in the case of both groups. The importance of this study is conferred by tomodensitometric information obtained both on the normal anatomy and on the pathological aspects of ICA, as well as the highlighting of ICA variations of origin, angle, length and trajectory. In this regard, radio imaging investigation reports should mention any variations in the trajectory of the ICA and note the sinuosities of the vessel, as well as the abnormal angles of the artery in relation to the CCA and the ECA.

Research on the anatomical variation of ICA is not extensive, but further studies could lead to the acceptance in the medical world of variations in anatomical indices as risk factors in the occurrence of atherosclerotic carotid disease. Further studies on flow divergences in the carotid bifurcation region and their correlation with zonal anatomy could lead to the implementation of new types of preventive treatment in the context of atherosclerosis, such as percutaneously fixed flow diverters. The detailed study of the anatomical variations of ICA can contribute to a better diagnostic conduct, by careful and early monitoring of patients in risk categories, as well as therapeutic decision by highlighting preoperative or preinterventional carotid abnormalities, ultimately ensuring low rates of neurovascular complications and a better standard of living for patients.

Thesis originality

Through this study we analyzed and detailed the complete morphometry on all ICA segments during the CT examination, providing information on calibers and dimensions, a study that has no correspondent in the literature.

We conducted studies that we did not find addressed in the research literature for the documentation of the study related to the morphology of the carotid sinus on CT, bringing current and targeted information.

We made correlations with statistical significance or not, supporting or refuting hypotheses regarding all anatomical parameters evaluated in the case of both study groups.

We also studied morphometric data on normal ICA or those affected by atherosclerotic pathology, some of them studied in the literature with similar results, which gives credibility to the conclusions of our study.

I believe that the importance of this study is also offered by the possibility to come to the aid of surgeons and internists, through detailed information about the normal anatomy but also about the pathological aspects of ICA.

The results of our study are also important for the imaging industries, providing guidance on what the report of an imaging examination of the carotid anatomy and pathology should contain.

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