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ORIGINAL ARTICLE

Extra- and intra-cranial arterial calcifications in adults depicted as incidental findings on cone beam CT images

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Abstract

Objective. The aim of this study was to evaluate, retrospectively, the gender- and age-related prevalence of incidentally found calcifications, depicted within the course of the extra- and intra-cranial portion of internal carotid artery (ICA), in cone beam computed tomography (CBCT) examinations in adults, and to assess their clinical significance. ***Materials and methods.*** Out of a pull of 700 CBCT examinations a total of 484 CBCT scans of adult patients were finally selected according to a set of pre-defined criteria. These were evaluated for arterial calcifications presence within the ICAs course according to gender and age criteria. ***Results.*** In total, 492 calcifications were detected: 211 (42.88%) extra-cranial and 281 (57.11%) intra-cranial. Those were recorded in 150 scans (30.99%) and 161 scans (33.26%), respectively. Calcifications, with either extra- or intra-cranial allocation, were found more frequent in males than in females (all p-values < 0.05); also patients who presented with positive findings were older than those without findings (all p-values < 0.05). Furthermore, calcification presence with either extra- or intra-cranial allocation increases with age (all p-values < 0.05). ***Conclusion.*** Significant calcification frequencies were found within the ICA's course, in CBCT scans. Moreover, an increased incidence of either extra- or intra-cranial presence of these depictions and its relation to age and gender was documented.

Key Words: *calcifications, carotid artery, cone beam computed tomography, internal carotid artery, diagnosis*

Introduction

The interpretation of the dental panoramic radiographs' (DPR) 2D images was—and in most cases still is—an indispensable diagnostic and treatment planning tool. The inclusion of the middle and the upper neck within the focal trough of a properly performed DPR have led—in the early 1980s—to the diagnosis of the arterial calcifications presence at the carotids area (usually referred as CACs) [1]. This has been documented further by many studies and has also been advanced significantly [2–9].

However, cone beam computed tomography (CBCT) is one of the most commonly used 3D-imaging procedures nowadays, which advances dental imaging and diagnosis significantly. CBCT examinations provide with 3D information about the structures relative position, overcoming the DPR 2D images inherent drawback, as it enables to both cover the volume of the head and include the entire maxillofacial area. As such, it is possible to detect abnormalities (in the form of incidentally found CACs) outside the specific region of interest. This is essential [10], particularly in cases that these findings are depicted in areas related to vital anatomical structures [11,12].

The presence of CACs in either the DPR or CBCT has recently been comprehensively reviewed [13]. It has also been suggested that the unilateral and bilateral calcifications' presence in the area of the carotids are among the most frequently calcified soft tissue finding [14]. Furthermore, in a series of 300 scans, calcifications in the carotid artery and within the internal carotid artery's (ICA) intracranial portion were found at 1.5% and 0.4% of the subjects, respectively [15]. The exact frequency and distribution of these findings vary widely across studies, depending on the field of view (FOV) used, the age groups,

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the studied population and the category of findings [15–19].

In addition, is has been well documented that CBCT provides accurate depiction in defining subtle structures (such as surgically relevant middle ear structures, the anatomy of the temporal bone and the lateral skull base) comparable to multi-detector computed tomography (MDCT) [20,21]. CBCT also provides high-contrast spatial resolution for sinus imaging, comparable with those shown by the MDCT [22]. It was also recently stated that visualizations of the laryngeal skeleton using MRI, as well as carotid atherosclerosis using CT, were similar to visualizations provided by CBCT [23].

Based on the above, the arterial calcifications presence and significance using CBCT have not been thoroughly investigated regarding either their intracranial allocation or their gender- and age-related prevalence.

This study aimed to evaluate retrospectively the gender- and the age-related prevalence of incidentally found calcifications depicted within the course of the extra- and intra-cranial portion of the ICA in CBCT examinations in adults and to assess their clinical significance.

This evaluation was based on a pre-defined set of criteria that characterize the presence of these calcifications.

Materials and methods

Subjects

Due to the retrospective design of the study, the subjects enrolled were of a series of 700 CBCT examinations recruited from the database of an imaging center in Athens, Greece, performed from October 2011 until March 2012. All cases were adult patients referred for: (a) complex orthodontic cases/orthognathic surgery, (b) obstructive sleep apnea (OSA)/airway assessment, (c) evaluation of facial trauma, (d) complex pre-surgical implant treatment planning and (e) control due to malignancy in their medical history records.

A total of 484 CBCT data sets was found to meet the including criteria that were: (a) subjects should be 40 years of age or older and (b) CBCT examinations had to be performed according to the maxillofacial protocol (full volume or large FOV). Images with movement or stripe artifacts were excluded. The age and gender of the studied population were recorded.

Ethics

The Ethics and Research Committee of the National and Kapodistrian University of Athens, School of Dentistry, approved our study's protocol (Ref.216/26.08.2013).

CBCT imaging

All examinations were performed with a NewTom VGi CBCT imaging unit (QR Systems, Verona, Italy) at 110 kV; 3.6 s exposure time and 2–5 mA (depending on the size of patient's head, average 18.4 mAs/patient). A reconstruction volume of 15 cm × 15 cm and a voxel size of 0.3 mm were also used. Reconstructions of the volumetric dataset were created by using the manufacturer's proprietary software NewTom Cone Beam 3D imaging, NNT Version 3.10 (QR srl., Verona, Italy).

Image evaluation

The examiners conducting this study were blinded to any existing medical and dental history information of the subjects and to prior clinical, histological or radiographic records, which might bias their opinion on the presence of a calcification.

A board of three (S.D., K.S. and K.T.) oral and maxillofacial radiologists (OMFRs) evaluated the scans individually and blind to each other. Any disagreement was solved in an iterative re-evaluation of the images until consensus was reached.

The OMFRs evaluated the scans for the presence of calcifications in the head and neck regions. The viewing procedure was standardized and performed by evaluating the multi-planar reconstructions of the volume under investigation. The interpretation procedure was based upon a pre-defined set of criteria that characterize the calcifications' presence, as reported in the literature [24–26]. These criteria were applied accordingly and also summarized and presented in Table I. Given that the maximum intensity projection (MIP) protocol provides with information about the calcifications' 3D location and extension, it was thought that it could assist in the evaluation of the findings.

Moreover, arterial calcifications were considered as positive findings when they were compatible with depictions located within the anatomical area of the course of the cervical part of the common carotid artery, up to its bifurcation and further distally within the lumen of external and internal carotid arteries. Thus, radio-opacities depicted within the aforementioned cervical portion of the artery until the internal carotid's entrance into the carotid canal in the skull base were considered to be extra-cranial calcifications within the arteries (CACs) (Figure 1). Any similar radio-opacity, depicted along the course of the internal carotid artery intra-cranially from the ascending part of the petrous portion up to the cavernous segment was recorded as an internal carotid artery calcification (ICAC). The findings were also documented on axial, coronal and sagittal projections. The aforementioned anatomical area of the ICA's intra-cranial course was thoroughly evaluated. This

Table I. The radiographic criteria of the CAC and ICAC justification.

	Reconstruction planes	Shape of radio-opacities	Location
CAC	Axial	Single or multiple 'rice grains'. Linear or curvilinear.	Cervical soft tissue area. Approximately 0–10 mm antero-laterally to the anterior tubercle of the transverse process. Lateral or more often lateroposterior to the greater cornu of the hyoid bone. Always postero-lateral to the pharyngeal airway space [25].
	Coronal		Lateral to the anterior tubercle of the cervical vertebrae [25].
	Sagittal		Medial and inferior to the angle of the mandible. Lateral and mostly anterior to the cervical tubercle. Vertical position varying from C3 to C5 [24,25].
ICAC	Axial	Single or multiple 'rice grains'. Tubular or curvilinear oblique structures.	Extended from the anterior to posterior clinoid process. Located laterally to the hypophysial fossa.
	Coronal	Single or multiple 'rice grains'. Characteristic oblique ring-like or 'figure eight' (8) shaped.	The lower part of the 'figure eight' is always depicted lateroposteriorly to the lower surface of the anterior clinoid process and extends lateroanteriorly, while the upper cycle is more medioanterior.
	Sagittal	Single or multiple 'rice grains'. Linear or curvilinear.	Along the petrous portion of the carotid canal in the temporal bone to the lacerum segment. Along the adjacent cavernous portion. On the medial side of the anterior clinoid process [26].

CAC, Carotid artery calcifications; ICAC, Internal carotid artery calcifications.

evaluation was made along the petrous portion of the carotid canal in the temporal bone to the lacerum segment, which begins above the foramen lacerum and ends at the petrolingual ligament. The ICA's intra-cranial course continues along the adjacent cavernous portion, where the artery is ascending toward the posterior clinoid process passaging by the side of the body of the sphenoid bone and again curving upward on the medial side of the anterior clinoid process. The S-shaped curve of the cavernous segment is called the 'carotid siphon' (Figure 2).

The characteristic radiographic depiction with which CAC and ICAC were presented in axial, coronal and sagittal reconstruction planes, along with the individually corresponding anatomic landmarks, are provided in Table I.

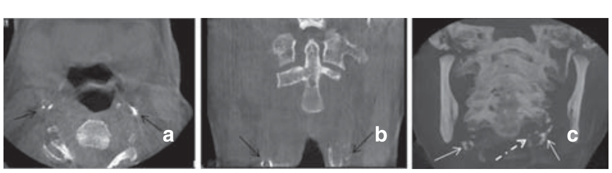

Figure 1. Extra-cranial calcifications within the arteries (CACs). (A) Axial projection of multiple 'rice grains', linear (left) or curvilinear (right) homogeneous radio-opacity (arrows), (B) coronal projection of the same patient; radio-opacities are located postero-lateral to the pharyngeal airway space and (C) maximum intensity projection (MIP) 3D reconstructed images showing the CACs arising laterally to the anterior tubercle of the cervical vertebrae bilaterally (arrows) and its medial-inferior relation with the angle of the mandible. Note the close proximity at the left side to the adjacent calcified superior cornu of the thyroid cartilage (dotted arrow).

In addition, as a pre-requisite, we characterized as positive findings the radio-opacities that were visible on a series of at least three sequential slices (axial and/or coronal and/or sagittal), that is 3-times the axial

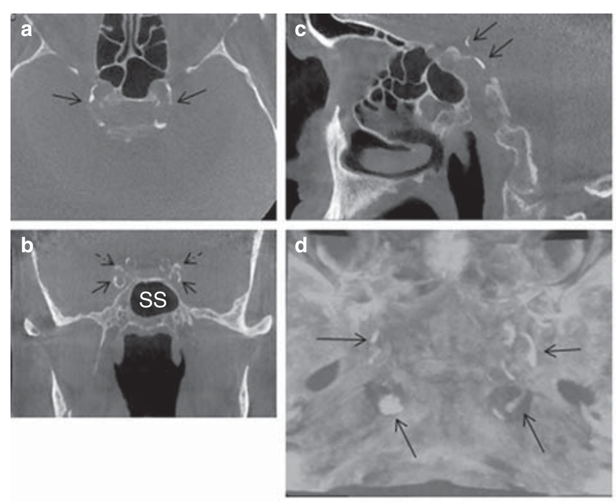

Figure 2. Intra-cranial calcifications of the internal carotid artery (ICAC). (A) Axial projection: an oblique tubular structure, extending from the anterior to the posterior clinoid process laterally of the hypophysial fossa (arrows); (B) coronal projection: multiple, extreme, curvilinear, homogeneous radiopacities (arrows). Note the characteristic oblique ring-like or 'eight' (8) shaped radio-opacity, depicted lateroposteriorly to the lower surface of the anterior clinoid process (dotted arrow) and lateroanteriorly to the upper part being more medioanteriorly; (C) sagittal projection: 'rice grains' shaped and linear masses depicted throughout the course of the internal carotid artery; (D) maximum intensity projection (MIP) 3D reconstructed image of the same patient, disclosing the ICACs (arrows) (SS: sphenoid sinus).

slice thickness (3 × 0.3 mm = 0.9 mm); in that manner, false positive findings as a result of imaging artifacts could be excluded.

Statistical analysis

The population of this study for each gender was sub-divided into five decade-based age-groups: 40–49 years, 50–59 years, 60–69 years, 70–79 years and 80–90 years of age. The results were evaluated by descriptive statistics. The chi-square test and *t*-test (significance level: $p < 0.05$) were used to evaluate the age-related significance of the extra- and intra-cranial calcifications presence within genders in each of the age-groups (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.).

Results

Out of the 484 data sets (scans), 214 were of males and 270 of females. The patients' age varied from 40–90 years of age; the mean age was 60.49 years of age. In total, 492 findings ($N = 492$) were identified.

CACs occurred in 30.99% of the scans ($n = 150$ out of 484 scans). The total of 211 CACs comprised 42.88% of all incidentally found calcifications ($n_1 = 211$ out of total 492 findings). Out of these, 18.90% were found in females ($n_2 = 93$; $N = 492$) and 23.98% in males ($n_3 = 118$; $N = 492$). These 211 CACs depictions were either right ($n_4 = 47$) or left sided ($n_5 = 42$) and also bilateral allocated ($n_6 = 61$; that is, two in each = 122). Either left- or right-sided, these calcifications were more prevalent in males than in females ($X^2 = 9.06$, df = 1, $0.003 = p < 0.05$ left; $X^2 = 6.11$, df = 1, $0.013 = p < 0.05$ right). Additionally, adults with either left- or right-sided CACs were older than those without any presence ($t = -7.79$, df = 482, $p < 0.05$ left; $t = -8.53$, df = 482, $p < 0.05$ right). Significant differences were also found in the frequencies of the left- or right-sided depictions with aging, within the studied age groups ($X^2 = 61.03$, df = 4, $p < 0.05$ left; $X^2 = 48.53$, df = 4, $p < 0.05$ right) (Table II).

Regarding the intra-cranially located calcifications, ICACs were recorded in 33.26% of scans ($n_7 = 161$ out of 484 scans). The total 281 ICACs comprised 57.11% of all incidentally found calcifications ($n_8 = 281$; $N = 492$). Out of these, 24.18% were of females ($n_9 = 119$; $N = 492$) and 32.92% were of males ($n_{10} = 162$; $N = 492$). Accordingly, 23 ICACs were found to be right-sided, 18 left-sided and 120 bilateral (i.e. again, these count twice, as both sided). Either left- or right-sided, ICACs were more prevalent in males than in females ($X^2 = 11.85$, df = 1, $p < 0.05$, left; $X^2 = 16.94$, df = 1, $p < 0.05$, right). Adults with either left- or right-sided ICACs were significantly older than those without any ICAC presence ($t = -9.56$, df = 482, $p < 0.05$, left; $t = -9.34$, df = 482, $p < 0.05$, right). Also, significant differences were found between the frequencies of either left- or right-sided ICAC depiction with increasing age, within the studied age-groups ($X^2 = 69.08$, df = 4, $p < 0.05$, left; $X^2 = 62.29$, df = 4, $p < 0.05$, right) (Table II).

Discussion

The aim of this study was to evaluate retrospectively the significance of the gender- and age-related prevalence of incidentally found calcifications, depicted within either the extra- or intra-cranial course of ICA in CBCT examinations.

The clinical significance of these calcifications' presence within the arterial wall has been well-documented by a plethora of studies [27–36].

Although the carotid arteries calcifications' presence in CBCT scans has been extensively investigated [11,14–19,24,25,37], no related article was found in the dental literature studying exclusively the age and gender relation to their presence. The majority of these articles provide *a priori* information regarding either the imaging characteristics of these findings [11,14,16,17,19] or their definition based on anatomical landmarks [24,25]. Only two of these articles [15,18] provide information about both the population studied and the diagnostic criteria applied; this was also stated in a recent systematic review [38].

Thus, the interpretation of our results was based firstly on the segregation and then to further evaluation of the data provided from the literature. This was made in terms of age distribution and categorization of findings. Any mismatch in our results, compared to those in the literature, can be logically attributed to the different age-populations and to the size of the FOV used.

The fact that we included in our study exclusively adults older than 40 years of age might seem an arbitrary choice. However, atherosclerosis is classed as a disease of aging and is also associated with premature biological aging [39,40]. Thus, we trust that our choice of specific age groups for inclusion criteria was pertinent.

Extra-cranial findings

Our results support the age- and gender-related prevalence in CACs depiction, using CBCT. A statistically significant correlation between age and gender with CACs was also found. We showed that the presence of CACs increases with age, as we found significant differences in the frequency of left- or right-sided CACs, related to age within the studied age-groups. Additionally, we found evidence that adults with either left or right CACs depictions are older than those without any presence of this finding. We also provided evidence that males are more prone

Table II. The gender and age distribution of extra- and intra-cranial findings.

	No of scans		ICAC						CAC					
			Males			Females			Males			Females		
Age group	Males	Females	Left	Right	Bilateral	Left	Right	Bilateral	Left	Right	Bilateral	Left	Right	Bilateral
40–49	32	44	0 (0.00%)	0 (0.00%)	2 (6.25%)	1 (2.72%)	0 (0.00%)	1 (2.72%)	1 (3.12%)	1 (3.12%)	2 (6.25%)	1 (2.72%)	0 (0.00%)	0 (0.00%)
50–59	67	80	2 (2.98%)	6 (8.95%)	11 (16.41%)	3 (3.75%)	5 (6.25%)	9 (11.25%)	7 (10.44)	8 (11.94%)	5 (7.46%)	4 (5.00%)	3 (3.75%)	4 (5.00%)
60–69	79	85	4 (5.06%)	5 (6.32%)	36 (45.56%)	3 (3.52%)	3 (3.52%)	12 (14.11%)	12 (15.18%)	12 (15.18%)	13 (16.45%)	5 (5.88%)	9 (10.58%)	6 (7.05%)
70–79	27	53	0 (0.00%)	0 (0.00%)	16 (59.25%)	4 (7.54%)	3 (5.66%)	22 (41.50%)	5 (18.51%)	2 (7.40%)	9 (33.33%)	6 (11.32%)	8 (15.09%)	14 (26.41%)
80–90	9	8	0 (0.00%)	1 (11.11%)	7 (77.77%)	1 (12.5%)	0 (0.00%)	4 (50.00%)	1 (11.11%)	3 (33.33%)	4 (44.44%)	0 (0.00%)	1 (12.5%)	4 (50.00%)
Mean age	Total	Total	6 (2.80%)	12 (5.60%)	72 (33.64%)	12 (4.44%)	11 (4.07%)	48 (17.77%)	26 (12.14%)	26 (12.14%)	33 (15.42%)	16 (5.92)	21 (7.77%)	28 (10.37)
60.49	214 (44.21%)	270 (55.78%)	Total^M (n_{10}) = 162 (32.92%)*			Total^F (n_9) = 119 (24.18%)*			Total^M (n_3) = 118 (23.98%)*			Total^F (n_2) = 93 (18.90%)*		
			Total ICACs (n_8) = 281 (57.11%)*						Total CACs (n_1) = 211 (42.88%)*					
							Total findings (N) = 492							
Total no of scans = 484			n_7 = 161 (33.26%)**						n = 150 (30.99%)**					

The percentages listed after the numbers of scans for each age-group refers to the number of findings per number of scans in that age-group.
ICAC, Internal carotid artery calcifications; CAC, Depictions located within the anatomical area of the course of the cervical part of the common carotid artery, up to its bifurcation and further distally within the lumen of external and internal carotid arteries.
The numbers and percentages listed after the n and n_7 refers to the number of scans and n_{1-10} refer to the number findings or accordingly.
*% of the total findings, ** % of the scans.

than females to show CACs—as these two variables were significantly correlated—regardless of the location of these findings.

Moreover, our findings regarding the bilateral CACs presence are closer to those of a study that presented 10.4% [37]. On the other hand, they are in disagreement with other published data, in which CACs were found in 1.5% of the scans [15], and also with those of a study that presented a 5.7% incidence of CACs [19]. It was recently documented that patients over 65 years of age are 5.01-times more likely to present vascular pathology (e.g. carotid artery calcification) than patients from 41–65 years of age and 13.39-times more than those from 16–40 years of age [18]. This corroborates our results regarding the statistical significance found between age and CACs.

Intra-cranial findings

ICACs were found in a considerable number of CBCT examinations. We found evidence that patients with either left or right ICAC depiction are older than those without any presence of this finding. Additionally, significant differences were documented between the frequencies of left- or right-sided ICACs depiction with increasing age. Males showed more ICACs after the age of 50 years. This frequency increases throughout the 6th, 7th and 8th decade in males, whilst females showed an almost linear increase after the age of 50 until the age of 80 and above.

This was probably due to the age-related increase of calcium deposition within the arterial wall, as already documented [27–32]. The latter proves the consistency of our results, as adults with either left or right ICAC or CAC signs were older than those without any presence of either ICAC or CAC. To the authors' knowledge, the dental literature has not yet provided evidence for age- and gender-related prevalence of atherosclerosis 'fingerprints' presence within the intra-cranial portion of the internal carotid artery's wall, using CBCT. Additionally, it was supported that severe calcification in the carotid siphon is correlated with a carotid siphon stenosis greater than 50% [33]. Also, a study conducted on the population-based Rotterdam study showed an overall ICAC prevalence of 82.2% [34].

Moreover, our results are different than those of a study reporting 0.5% [15] that rather under-estimated the clinical significance of this finding. They are also different than those presented in a most recent study that separated into ICACs located in the middle cranial fossa (8.49%) and into the cavernous sinus section (3.14%) [18]. The incidence presented in the current study is obviously greater.

This study documents an overall high prevalence of total CACs and ICACs, as well as an age-related distribution that may be higher in percentages than those reported elsewhere in the dental literature [15,18], but, in the meantime, are still lower if compared with those provided by other studies [29–31,33,34]. Hence, we have probably under-estimated in our study the real amount of intra-cranial atherosclerosis.

Primarily, one may argue that we include in our study OSA patients whose CBCT data originated from a large FOV. As it has been demonstrated, no substantial benefit exists for patients specifically referred for OSA evaluation [41]. Second, OSA patients are more prone to develop atherosclerosis [42] and definitive sleep apnea diagnosis and assessment is usually performed in a sleep lab [43]. However, our study comprised subjects that were referrals, the anonymity of which was protected by codification along with the exclusion and inclusion criteria. Additionally, the OMFRs were blinded to the subjects' potentially existing medical and dental history information, as described in the methodology section. Thus, we considered these cases as part of the general (anonymous) adult population; so its presence did not affect the final outcomes. Additionally, the accuracy of CBCT in atherosclerosis depiction remains to be investigated.

This is important to realize, as the major role of intra-cranial atherosclerosis as a cause of cerebrovascular disease was recently shown [35,36]. This translates to the fact that people who did not present CACs and/or ICACs in CBCT scans may still have atherosclerosis.

Dentists are generally aware of CACs depiction in DPRs as 2–4.5% of patients' aged over 50 years present this finding [44]. It is also known that its prevalence increases up to 22–37% when an underlying pathology (such as hypertension, type 2 diabetes, smoking, hypercholesterolemia, history of cardiovascular disease, obstructive sleep apnea syndrome, metabolic syndrome, menopause and neck radiotherapy) is present [2–9,45]. This also delineates accordingly the diagnostic task in case of a CAC or ICAC presence within the CBCT examination. Unfortunately, as only the patients' CBCT data were available for retrospective evaluation in our study, no co-evaluation of the patients' DPRs was possible to be performed. The latter, regarding the incidence of CACs' depiction in either DPR or CBCT (no longer in the form of IF [13]), but in its' inter-relation concerning these findings' depiction remains to be investigated in well-designed future studies.

As an overall high prevalence of CACs and ICACs presence in CBCT examinations was documented in our study, significantly higher than those of DPR, we recommend a thorough evaluation of the total CBCT volume available for these calcifications presence. This is also revealed by a consortium of OMFRs and medical radiologists, as its presence in the form of CACs represents the 'tip of the iceberg' and a later manifestation of an already mature atheroma that has been associated with a high risk of cerebral emboli [13]. Accordingly, these patients have to be referred for further medical evaluation, as they comprise a subgroup completely different than patients that cardiologists or other medical specialists usually refer to.

In conclusion, significant calcifications' frequencies were found within the extra- and intra-cranial course of ICA in CBCT scans. Moreover, an increased incidence of CACs and ICACs depictions related to age and gender was documented. We submit that CBCT examinations, meticulously assessed in their total volume, lead to more frequent arterial calcifications detection than what is hitherto known. Most importantly, their depiction can serve as a presence indicator of the well-known predisposing factors.

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