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The effect of vertebral artery characteristics on cervical discogenic pain and disability

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ABSTRACT

Objective : Cervical discogenic pain, which is characterized by a stiffness or pain in neck movement, generally occurs as a result of disc degeneration. On the other hand; vascular pathologies of the cervical region, especially vertebrobasilar insufficiency, may give rise to similar findings in patients; it can also be detected simultaneously with cervical disc pathologies. In this study, it was aimed to investigate whether the circulatory properties of the vertebral arteries have an effect on the neck pain and functional status of the patients.

Material and Method: Based on the participants' medical history, physical examination and radiological examination, sixty five patients were diagnosed with cervical disc herniation. Twenty patients who met the inclusion criteria were completed the study. Vertebral artery and carotid artery doppler ultrasonography was performed in these patients, thus any stenosis or insufficiency in vascular systems of the neck was evaluated. Additionally; vertebral blood flow rate (ml/min),vessel diameter(mm), minimum blood flow velocity (Vmin) and maximum blood flow velocity (Vmax) was measured by doppler ultrasonography. The obtained findings compared with patients' level of pain measured with the "VAS (Visual Analog Scale)" and the level of daily life activities measured by the "Neck Disability Index ".

Results: It was detected a statistically significant negative correlation between the VAS score and right vertebral artery diameter ($p=0.019$, $r=-0.518$). A significant reverse correlation between VAS score and right vertebral arterial blood flow rate ($p=0.011$, $r=-0.556$) was also observed. No correlation was found between other vertebral artery parameters and VAS score or Neck Disability Index ($p>0.05$).

Conclusion: The findings of this study revealed that there is a correlation between the vertebral artery flow rate and pain level. Clinicians must take into consideration vertebral pathologies in patients with neck pain because of this vital condition may accompany with various musculoskeletal pathologies such as cervical disc herniation.

Keywords: Vertebral artery, neck pain, disc herniation, cervical vertebrae.

INTRODUCTION

Cervical discogenic disorder is a major medical problem in the general population. The prevalence of the disease has increased with regard to age in both genders especially between the third and fifth decades (1,2).This clinical syndrome is characterized as a displacement of the nucleus pulposus in the intervertebral disc; as a result, the impingement of the cervical nerves may be formed at the exit section of the neural foramen or the compression of the spinal cord can be situated in the spinal canal (3).

Cervical discogenic pain, which is characterized by a stiffness or pain in neck movement, generally occurs as a result of disc degeneration (4). Symptoms are usually worsened by activities in which the neck is held in the same position for a long time such as working on a computer, reading, writing, driving, etc. (4). The pain caused by disc herniation is due to the disruption in the disc structure and the imbalance of the pressure distribution between the disc, vertebra endplate and facet joints (4). Such pain is mostly mechanical and local inflammation may also co-occur with the clinical condition (4). Besides the patients' symptoms, physical examination findings and magnetic resonance examination evidences also support the diagnosis.

The compressive forces caused by cervical disc herniation may also give rise to various degrees of microvascular damage by a venous obstruction that results in congestion

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and edema, which can lead to arterial ischemia (3). The circulation of the cervical spinal cord occurs mainly through the vertebral artery in which the development of circulatory findings or having circulatory diseases may increase the patient's complaints (5). Neck pain, ipsilateral arm pain, cervical paravertebral muscle spasm, restriction of cervical movement and paresthesias related to dermatomal dispersion are among the common symptoms of the cervical disc herniation that can lead to serious disabilities among patients (3,6). On the other hand; vascular pathologies of the cervical region, especially vertebrobasilar insufficiency, may give rise to similar findings in patients; it can also be detected simultaneously with cervical disc pathologies.

Vertebrobasilar insufficiency is a vascular pathology which is characterised by insufficient blood flow of the posterior circulation system supplied by two vertebral arteries that constituted the basillar artery (7). There are many risk factors including age, smoking, hypertension, hyperlipidemia that increase the likelihood of developing atherosclerosis for the vertebral artery insufficiency (7). This pathology can also lead to a number of neurological symptoms as vertigo, diplopia, dizziness, ataxia, headache, motor weakness in addition to neck pain (7). It may be the precursor of many pathologies such as medullary syndrome, posterior cerebral artery occlusion, cerebellar infarction, locked in syndrome (7) . Since vertebrobasilar insufficiency is a vital clinical condition and may exacerbate patients' clinical symptoms; it is essential to perform vascular examinations in patients with these symptoms.

There are many options in the treatment of cervical disc herniation including medications, physical therapy modalities, exercise practices and surgical treatment methods. However, some of the patients diagnosed with cervical disc herniation do not benefit from all of these treatments and it is observed that their complaints are ongoing. This situation has led us to investigate whether there are other underlying factors that may affect the level of pain in patients with cervical disc herniation. The most vital condition among these factors that shouldn't be ignored is the circulatory pathologies in the vertebral artery. In this study, it was aimed to investigate whether the circulatory properties of the vertebral arteries have an effect on the neck pain and functional status of the patients. To the best of our knowledge, this is the first study to evaluate the effect of vertebral artery parameters on cervical pain and disability in patients who were diagnosed with cervical disc herniation. By the results of this study, it was aimed to increase the awareness of clinicians on this issue. It was also intended to emphasize that in patients with a diagnosis of cervical disc herniation, the source of pain may not originate only from the musculoskeletal system.

MATERIAL AND METHOD

This prospective, observational study was performed at a tertiary hospital and intended to investigate the influence of vertebral artery characteristics on pain intensity and physical function between May 2018 and May 2019. All participants signed the informed consent form. This study was approved by Karabuk University Non-interventional Clinical Researchs Ethics Committee (Date: 02.05.2018, Decision No: 5/6). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The participants of the study were selected from patients diagnosed with cervical disc herniation as reflected in their medical history, physical examinations and magnetic resonance imaging (MRI) findings. The participants who experienced complaints such as dizziness, headaches, diplopia, blindness, imbalance, numbness, weakness and who had risk factors of hypertension, diabetes mellitus, hyperlipidemia, family history for cardiovascular diseases, smoking and obesity were included in the study. Vertebral artery and carotid artery doppler ultrasonography was performed in these patients, thus any stenosis or insufficiency in the vascular systems of the neck was evaluated. Moreover; vertebral blood flow rate (ml/min), vessel diameter (mm), minimum blood flow velocity (Vmin) and maximum blood flow velocity (Vmax) was measured by performing doppler ultrasonography. The patients' level of pain was measured by using a 100 mm Visual Analog Scale (VAS) score and the level of daily life activities was detected by the Neck Disability Index. These values were also compared according to the patients' demographic characteristics, comorbidities, body mass index values. It was investigated whether there was a significant difference between the specified values.

There are many clinical instruments available for assessing disability in cervical discogenic disorders. The Neck Disability Index, which is the first created scale for neck pain related disability, is the most commonly used self report instrument for evaluating status of neck pain related disability in clinical researches (8-11). The instrument is a disease-specific scale for assessing pain intensity, personal care, headaches, concentration, sleeping, recreation, lifting ability and neck pain induced by reading, working and driving (12).

Based on the participants' medical history, physical examination, and radiological examination, sixty five patients were diagnosed with cervical disc herniation and twenty patients who met the inclusion criteria were included and completed the study. The inclusion criteria for the participants were as follows:

(1) Being 18 years old or older

(2) Being diagnosed with cervical disc herniation with no advanced herniation and no nerve compression at

the level of extrusion or sequestration in the current MRI in addition to incidences of neck pain

(3) Having one or more symptoms of vertebrobasilar insufficiency such as headache, nausea-vomiting, dizziness, diplopia, syncope, vision problems, balance problems, numbness and loss of strength

(4) Having one or more of the risk factors for circulatory disorders such as rheumatic disease, migraine, hypertension, cigarette addiction, obesity, atherosclerosis, history of embolism, artery dissection, coagulopathy, fibromuscular dysplasia and Takayasu arteritis

(5) Having no signs of stenosis or failure in the carotid artery doppler examination

(6) Having no history of trauma

(7) Being willing to participate in the study

On the other hand, the exclusion criteria were as follows:

(1) Having major general health problems (e.g., heart failure or chronic obstructive pulmonary disease), metabolic disorders, acute or chronic infectious disorder and malignancy

(2) Having pregnancy

(3) Refusing to participate in the study

The flow chart of the study is presented in **Figure 1.**

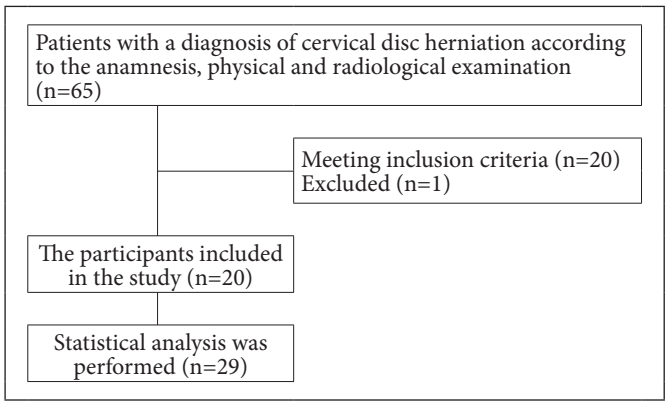

Figure 1. The Flow Chart of the Study

Statistical analyses were performed using the version 22.0 of SPSS software (IBM Corp., Armonk, NY, USA). The conformity of univariate data to normal distribution was evaluated by Kolmogorov-Smirnov test and Shapiro-Wilk Francia test; while variance homogeneity was evaluated with Levene test. Mann-Whitney U test and Exact results were used together in comparing two independent groups according to quantitative data. Spearman's rho test was applied to examine the correlations of variables. Bagging Linear Regression analysis was used to reveal the causality between the dependent variables (Visual Analog Scale and Neck Disability Scale) and other independent variables. Median value was determined as the coupling parameter. Information criterion (AICC) method in forward stepwise method was selected from the model selection methods. Neural Network (Multilayer Perceptron) as one of the consulting machine learning methods was used to find and estimate the most important independent variable with dependent variables (Visual Analog Scale and Neck Disability Scale). Gradient descent was selected for optimization algorithm. Hyperbolic tangent was applied for hidden layer activation function and identity was used for output layer activation function. Mini-Batch method was used for training data selection and calibrated as 70% vs 30% for training and testing sets respectively. Quantitative variables are determined as mean±SD (standard deviation) in tables and median (minimum/maximum); while categorical variables were shown as n (%). Variables were analyzed with a 95% confidence level and p value of less than 0.05 was considered as significant.

RESULTS

The mean age of the participants was 45.95±14.86 years. Majority of the participants were female with a ratio of 90 % (n=18) and 10% were male (n=2). The mean value of BMI was found to be 27.37±3.58. The duration of neck complaints was 10.45±1.49 months. The patient characteristics are presented in **Table 1** and **Table 2**.

Table 1. The characteristics of the participants

	Mean (SD.)	Median (Min/Max)
Age	45.95 (14.86)	43 (23/72)
BMI	27.38 (3.58)	28.65 (19/32.4)
	N	**%**
Gender		
Female	18	90.0%
Male	2	10.0%
Smoke		
No	18	90.0%
Yes	2	10.0%
Comorbidity		
No	6	30.0%
Yes	14	70.0%
Diabetes	3	15.0%
Asthma	2	10.0%
Hypertension	1	5.0%
Gastritis	1	5.0%
Hypothyroidism	1	5.0%
Diabetes+Gastritis	1	5.0%
Diabetes+Hypertension	2	10.0%
Asthma+Vertigo	1	5.0%
Hypothyroidism+Migraine	1	5.0%
Hypertension+Depression	1	5.0%

SD.: Standard deviation, n: Number of participants

Table 2. The complaints of the participants

Patient complaints	n	%
Neck pain+Numbness in upper extremity	10	50.0%
Neck pain+Numbness in upper extremity+Dizziness	2	10.0%
Neck pain+Dizziness+Headache	2	10.0%
Neck pain+Dizziness	2	10.0%
Neck pain+Loss of strength in upper extremity	1	5.0%
Neck pain+Numbness in upper extremity+Double Vision	1	5.0%
Neck pain+Earache+Dizziness	1	5.0%
Neck pain+Headache	1	5.0%

n: Number of participants

The vertebral artery characteristics of the patients were also analyzed. Vessel differentiation was also observed along with the bilateral vertebral arteries' diameter, minimum blood flow velocity (Vmin), maximum blood flow velocity (Vmax) and blood flow rate (ml/min). The mean values of the vessel diameters of the right and left arteries were 4.89±7.1 and 4.2±5.8 respectively. The mean blood flow rates of the right and left vertebral arteries were 2.60±0.46 and 2.89±0.32 respectively. The mean values of the Vmax and Vmin of the right vertebral artery were 39.40±16.29 and 11.10±3.58 whereas that of the left vertebral artery were 42.25±12.83 and 14.0±6.03 respectively. The vertebral artery characteristics of the participants are presented in **Table 3**.

Table 3. The vertebral artery characteristics of the participants

	Right Vertebral Artery Mean (SD.)	Left Vertebral Artery Mean (SD.)
Vessel Diameter (mm)	4.89±7.1	4.2±5.8
Minimum Blood Flow Velocity (Vmin)	11.1±3.6	42.25±12.83
Maximum Blood Flow Velocity (Vmax)	39.4±16.2	14.0±6.03
Blood Flow Rate (ml/min)	78.5±44.4	101.0±42.3

SD.: Standard Deviation

Based on the analysis of the pain and neck disability levels, it was shown that the mean value of VAS scores was 36.25±32.5 and that of the Neck Disability Index scores was 16.6±5.78. It was detected a statistically significant negative correlation between the VAS score and right vertebral artery diameter (p= 0.019, r=-0.518). A significant reverse correlation between the VAS score and right vertebral arterial blood flow rate (p=0.011, r=-0.556) was also observed (**Figure 2** and **Figure 3**). No correlation was found between other vertebral artery parameters and VAS score (p > 0.05). Furthermore, no correlation between the Neck Disability Index scores and vertebral artery characteristics was found (p > 0.05) (**Table 4**).

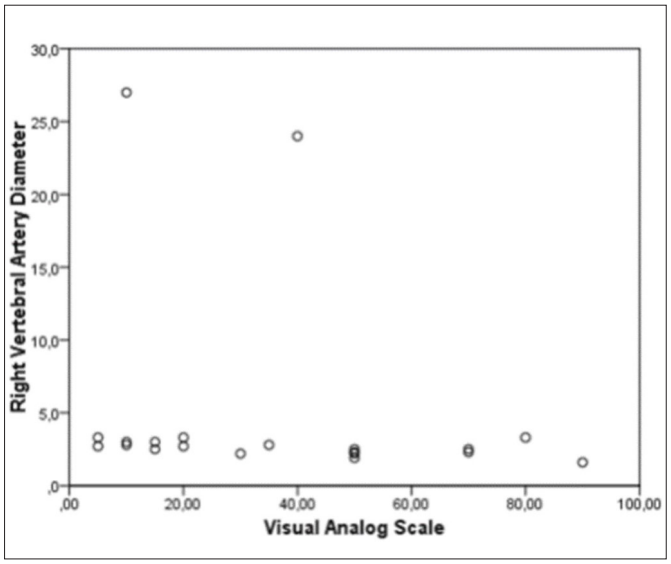

Figure 2. The Correlation between Right Vertebral Artery Diameter (mm) and VAS Level

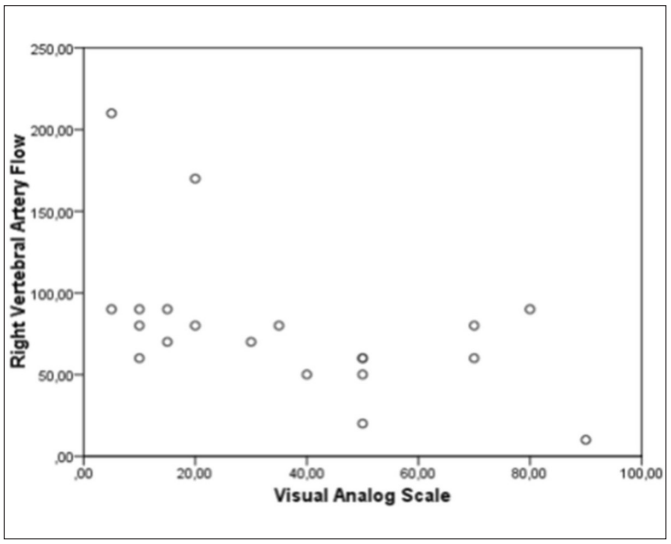

Figure 3. The Correlation between Right Vertebral Artery Flow Rate (ml/min) and VAS **Level**

Table 4. The Correlation table of the study findings (Spearman's rho Test)

	Neck Disability Scale		Visual Analog Scale	
	r	p	r	P
Age	-0.240	0.307	-0.165	0.487
BMI	0.190	0.422	0.184	0.438
Right Vertebral Artery Diameter	0.449	0.050	-0.518	0.019
Right Vertebral Artery Flow	0.318	0.172	-0.556	0.011
Right Vertebral Artery Vmax	0.051	0.831	-0.188	0.427
Right Vertebral Artery Vmin	0.144	0.546	-0.304	0.192
Left Vertebral Artery Diameter	-0.244	0.299	0.268	0.253
Left Vertebral Artery Flow	-0.372	0.106	0.110	0.644
Left Vertebral Artery Vmax	-0.254	0.280	0.073	0.759
Left Vertebral Artery Vmin	-0.241	0.307	-0.197	0.404
Total Vertebral Artery Flow Rate	0.085	0.723	-0.258	0.271

r: correlation coefficient, p: probability value (p value)

According to the Neural Network (Multilayer Perceptron) analysis, which is used to estimate the effects of variables on the Visual Analog Scale; the significance rates of the variables were 12.5% for right vertebral artery Vmin, 11.4% for left vertebral artery Vmax ,10.5% for duration of pain (months), 10.1% for right vertebral artery Vmax, 9.3% for right vertebral artery flow, 7.8% for left vertebral artery Vmin, 7.0% for right vertebral artery diameter, 6.3% for total vertebral artery flow rate, 5.4% for comorbidity, 4.4% for left vertebral artery flow, 3.3% for smoke, 2.8% for left vertebral artery diameter, 2.6% for age, 2.6% for BMI, 2.5% for family history and 1.4% for gender variables. The prediction success of the model was calculated as 99.9% (**Table 5**).

Table 5. Significance ratios of variables on the Visual Analogue Scale and Neck Disability Index

	Visual Analog Scale (D.V.)	Neck Disability Scale (D.V.)
Independent Variable	**Importance**	**Importance**
Gender	1.4%	0.8%
Smoke	3.3%	5.1%
Comorbidity	5.4%	2.0%
Family History	2.5%	1.5%
Age	2.6%	6.2%
BMI	2.6%	8.2%
Right Vertebral Artery Diameter	7.0%	11.4%
Right Vertebral Artery Flow	9.3%	12.1%
Right Vertebral Artery Vmax	10.1%	5.7%
Right Vertebral Artery Vmin	12.5%	4.4%
Left Vertebral Artery Diameter	2.8%	11.1%
Left Vertebral Artery Flow	4.4%	12.5%
Left Vertebral Artery Vmax	11.4%	3.5%
Left Vertebral Artery Vmin	7.8%	6.3%
Total Vertebral Artery Flow Rate	6.3%	3.1%
Duration of pain (months)	10.5%	6.1%
n (%) : Training/Testing	20(100)/0(0)	20(100)/0(0)
Percentage of correct predictions: Training/Testing	99.9	99.9

Neural Network (Multilayer Perceptron), Hidden layer activation function: Hyperbolic tangent, Output layer activaction function: identity, DV: Dependent Variable

DISCUSSION

In the pathophysiology of cervical disc herniation; a clinical formation occurs as a result of the progression of the nucleus pulposus inside or under the posterior longitudinal structures due to the rupture of annulus fibrosus (13). On the other hand, the neck is an important area because of the large number of vessels and nerves in the vertebral column (14). Thus, additional pathologies can contribute to the severity of neck pain in patients with cervical disc herniation; thus vascular pathologies are of primary importance under these conditions. Vertebrobasilar insufficiency, which is one of these vascular problems, is a serious medical condition that should not be ignored in diagnosis.

Vertebral arteries allow the distribution of essential nutrition to the cervical spinal cord, making it the first and largest branch of the subclavian artery (5,15,16). They are located on both sides of the posterior neck and form the basillary artery at the base of the skull by circulating in the neural foramens between the first and seventh cervical vertebrae (17). The normal value of the total volume in bilateral vertebral arteries is over 200 ml/min and the decreased blood flow rate (less than 200 ml/min) is an indicator of vertebrobasilar failure (17). Atherosclerosis, embolism, arterial dissection, coagulopathies, fibromuscular dysplasia, migraine and substance abuse are among the causes of vertebrobasilar insufficiency; additionally, hypertension, cigarette addiction, and obesity are thought to be the main risk factors (18-20).

Many studies in the literature show that ischemic pathologies give rise to pain in the musculoskeletal system (21-26). These studies have shown that the amount of oxygen supplying the metabolic needs of the surrounding tissues is not provided adequately as a result of the decrease in blood flow in the skeletal muscle (21,27-33). It is also hypothesized that the obstruction of perfusion is the main reason for the pain experienced by the patients (21,32,34,35). In a review by Queme et al. it was also revealed that factors relating to the up-regulation of growth factors and cytokines within the muscles during ischemic conditions and microvascular changes may be linked to the over-expression of different receptor molecules in the dorsal root ganglia which will in turn modulate pain and sympathetic reflexes as observed in the recent evidences (21). It is suggested that the afferent sensitization due to ischemia is related with the interplay between the transient receptor potential channels, acid sensing ion channels, and purinergic (P2X and P2Y) receptors in sensory neurons (21,36).

There was a female predominance in our study which was in accordance with literature. In a study by Gaigalaite et al. it was revealed that vertebral artery hypoplasia was more common in women (33 %) rather than in men (23.5 %) and vertebral artery was found to be wider in males than in females (37). Similarly, the findings of another study by Schievink et al. which determines the long term follow up of patients with spontaneous recurrent cervical artery dissections showed that most of the patients with dissections of both vertebral artery and internal carotid artery were women (85%)(38). Singuim et al. also specified that the risk of vascular disease increases during menopause as a result of the decrease in endogenous estrogens, which reduces the risk of serious vascular events in their study (39). Additionally, they stated that the development of hypertension and diabetes during pregnancy will give rise to an increase for the risk of vascular disease in the future periods of their life (39).

To the best of our knowledge, this is the first study that investigates the influence of vertebral artery parameters on cervical pain and disability. In this study, it has found a significant reverse correlation between the right vertebral artery flow rate and VAS level. However, any correspondence between the left vertebral artery characteristics and VAS level wasn't found in our study. This could be due to the mean flow rate of the right vertebral artery being below the normal value of 100 ml/min; while the mean flow rate of the left vertebral artery is above the normal value of 100 ml/min. We hypothesized that the left vertebral artery, which has a normal mean value of blood flow rate, does not affect pain formation as it contributes to the adequate blood supply of the musculoskeletal structures on the left side of the neck. On the other hand, more clinical studies are needed to generalize the results obtained from this study.

While the present study achieved its intended objectives, limitations were also considered in terms of the small number of participants due to the application of the comprehensive inclusion criteria and territorial limits which includes the generalizability of these findings to other ethnic groups. However, this study can guide future studies because of the findings were able to present the clinical data and the direct complaints of the participants.

CONCLUSION

Overall, the findings of this study revealed a correlation between the vertebral artery flow rate, diameter and pain level. Vertebral artery pathologies are serious clinical conditions and a delay in diagnosis may cause a detrimental impact on the patients' vital functions. Clinicians must take into consideration vertebral pathologies in patients with neck pain, wherefore this vital condition has a tendency to co-occur with various musculoskeletal pathologies, such as cervical disc herniation.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved by Karabük University Non-interventional Clinical Researchs Ethics Committee (Date: 02.05.2018, Decision No:5/6).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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