



Original Article

Cavum velum interpositum cysts in normal and anomalous fetuses in second trimester of pregnancy: Comparison of its size and prevalence

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ABSTRACT

Objective: Cavum veli interpositi (CVI) is a potential space below the splenium of corpus callosum and sometimes presents as a cyst.**Materials and methods:** In this prospective cross-sectional study, 360 fetuses with normal second trimester scan and 152 s trimester fetuses with structural abnormalities were included.**Results:** The CVI cysts were more common in fetuses with brain anomaly compared to normal fetuses and fetuses with extra-central nervous system (CNS) anomalies (23% vs 18.3% and 18% respectively; p value < 0.01). The mean size of cysts in normal fetuses, fetuses with extra-CNS anomalies and fetuses with brain abnormalities was 4.6 mm, 5.8 mm and 9.2 mm respectively. There was a significant difference between cysts size in normal fetuses and fetuses with brain anomalies (p value < 0.01) and the cut-point was 7.1 mm.**Conclusion:** The prevalence of CVI cysts is more in fetuses with brain anomaly. Fetuses with a cyst size >7.1 mm need a more detailed brain examination.© 2019 Taiwan Association of Obstetrics & Gynecology. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Cavum veli interpositi (CVI) is a potential space located in midline superior to the tela choroidea of the third ventricle, antero-inferior to the splenium of the corpus callosum and under the columns of the fornices. It is in communication with the sub-arachnoid space, lined by leptomeninges and represents an anterior extension of the quadrigeminal plate cistern above the pineal gland and internal cerebral veins. If this potential space is dilated and fluid filled it results in the CVI cyst [1–3]. It is still unclear whether isolated CVI cysts are a normal variant or developmental malformations [3].

It is a frequent finding in about 21–34% of children less than 2 years [1] but after that, it has been reported in only about 2–5.5% [4,5]. But it has been rarely reported in fetal period with a mean diameter of about 10–12 mm in literature [3,6].

Furthermore, the clinical importance of CVI cysts is uncertain but in most studies, isolated cysts were usually associated with favorable postnatal outcome [3,4,7].

The cause of the difference between the mentioned incidence in prenatal and the infancy period is unknown. Is this a late finding during pregnancy or has a really less prevalence in this period? In this study, our main aim was to evaluate and compare the prevalence rate and size of CVI cysts in normal fetuses and anomalous fetuses in the second trimester of pregnancy. We also followed the cysts in most of the normal fetuses for assessment of the outcome in prenatally detected isolated cysts.

Method

The present research was a prospective cross-sectional study and was done between 2016 and 2018 at teaching Yas women's hospital. Our institutional ethics board approved this study and informed consent was obtained from all individual participants. During the study period, 360 fetuses with normal second-trimester scan and 152 fetuses with structural abnormalities at second

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trimester (who referred for legal termination) were included. The second ones were categorized into fetuses with CNS anomalies (73 cases) and fetuses with extra-CNS anomalies (79 cases). The fetuses with a gestational age less than 16 weeks were not included (Fig. 1).

All participants had a single pregnancy. The exclusion criteria in normal fetuses were the presence of fetal anomalies during the study, increased risk of the first trimester combined screening and fetal weight less than 10%. In anomalous fetuses, all structural abnormalities either in brain or extra-CNS were included. Gestational age was calculated based on the crown-rump length (CRL) resulted from first trimester sonography between 10 weeks and 13 weeks and 6 days. All measurements were carried out by a Trans-abdominal convex array transducer with 2–6 MHz frequency (Affiniti 50, General imaging configuration, Philips ultrasound machine, USA). The fetal brains were evaluated in axial, sagittal and coronal planes to evaluate the size and location of the cysts and associated anomalies. Based on the previous study by Chen et al., in 1998 the internal cerebral veins are located either inferior or inferolateral to these cysts at sonography. So the location of the cyst in relation to the internal cerebral veins was assessed and confirmed by color Doppler study (Fig. 2). In anomalous fetuses the type of anomalies was recorded as well. The follow up data of the majority (60%) of normal fetuses were available and included in the result. All of anomalous fetuses were referred for legal termination because of multiple or complex anomalies, so they were not followed up.

All collected data were analyzed by using the statistical software SPSS 22. A *p* value of less than 0.05 was considered statistically significant. In order to determine the cut-off point to separate the size of cysts in normal fetuses from the fetus with CNS anomaly, Receiver Operation Characteristic (ROC) curve test was used.

Results

In this study, 360 normal fetuses compared with 152 anomalous cases with nearly similar gestational age range: 17–23 weeks (average age: 18 weeks + 6 days) in normal fetuses and 16–19 weeks (average age: 18 weeks) in other groups. Among normal fetuses, 66 of them and among fetuses with the anomaly, 32 of them had CVI cysts.

The mothers' average age in fetuses with CVI cyst in normal group was about 31.4 ± 6 years old and in fetuses with anomaly was about 31.8 ± 7 years old, and in anomalous fetuses without CVI cyst was 30.9 ± 7 years old.

There was no statistically significant difference between gender percentage in normal fetuses with CVI cyst (Male: 33, Female: 33, *P* value > 0.05) and anomalous fetuses without cyst (Male: 62, Female: 58, *P* value > 0.05). But in anomalous fetuses, the cyst was more common in male fetuses (Male: 22, Female: 10, *P* value = 0.03).

The CVI cysts were more common in fetuses with CNS anomaly compared to normal fetuses and fetuses with extra-CNS anomalies (23% vs 18.3% and 18% respectively; *p* value < 0.01) (Table 1).

In some anomalous fetuses, only one kind of anomaly was detected and in others, there were several types of anomalies. The most common brain anomaly in fetuses with cyst was Dandy-Walker spectrum (49.9%) (Fig. 3) include Dandy-Walker malformation, vermian hypoplasia, and black's pouch cyst and then Arnold-Chiari malformation (16.6%). In fetuses without cyst, ventriculomegaly (34.6%) was the most common and then Dandy-Walker spectrum (26.8%). There was a significant difference between the prevalence of ventriculomegaly in two groups (34.6% vs 5.5%, *P* < 0.05) and was much lower in fetuses with a cyst (Table 2).

The most common extra-CNS anomaly in fetuses with and without cyst was related to cardiovascular structures (26.9% and 28.5% respectively) and then abdominal organs (23% and 22.5% respectively) (Table 3).

The mean size of CVI cysts in normal fetuses was 4.6 ± 1.1 mm (3–9.5 mm). Also in fetuses with brain abnormality, it was 9.2 ± 3.7 mm (3.3–16 mm) compared to 5.8 ± 1.9 mm (3.9–9.7 mm) in fetuses with extra-CNS anomalies. There was a significant difference between cysts size in normal fetuses and fetuses with brain anomalies (*p* value < 0.01). The cut-point of CVI cysts was 7.1 mm with a sensitivity of 70%, the specificity of 98%, the positive predictive value of 92%, the negative predictive value of 92% and accuracy of 92% (Fig. 4). In the normal group, only 3 cases had cyst size larger than 7.1 mm and in these cases, the cysts were resolved during pregnancy, one in 25 weeks and one in 32 weeks, and the last case after birth.

About 60% (40 cases) of all normal fetuses were followed, and in all of them cysts were resolved during pregnancy or after birth without any new abnormalities during follow up.

Discussion

Based on embryology, the CVI is a true cistern in the roof of the third ventricle. It is not clear which pathophysiological mechanism results in cystic dilatation of this structure. It could be a result of

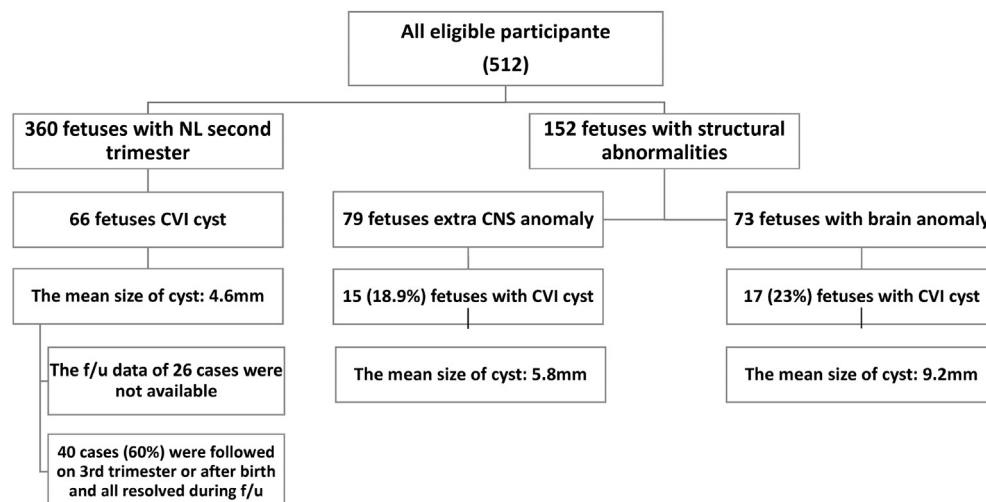


Fig. 1. Flow chart of the study design. CVI, Cavum velum interpositum; CNS, Central Nervous System.

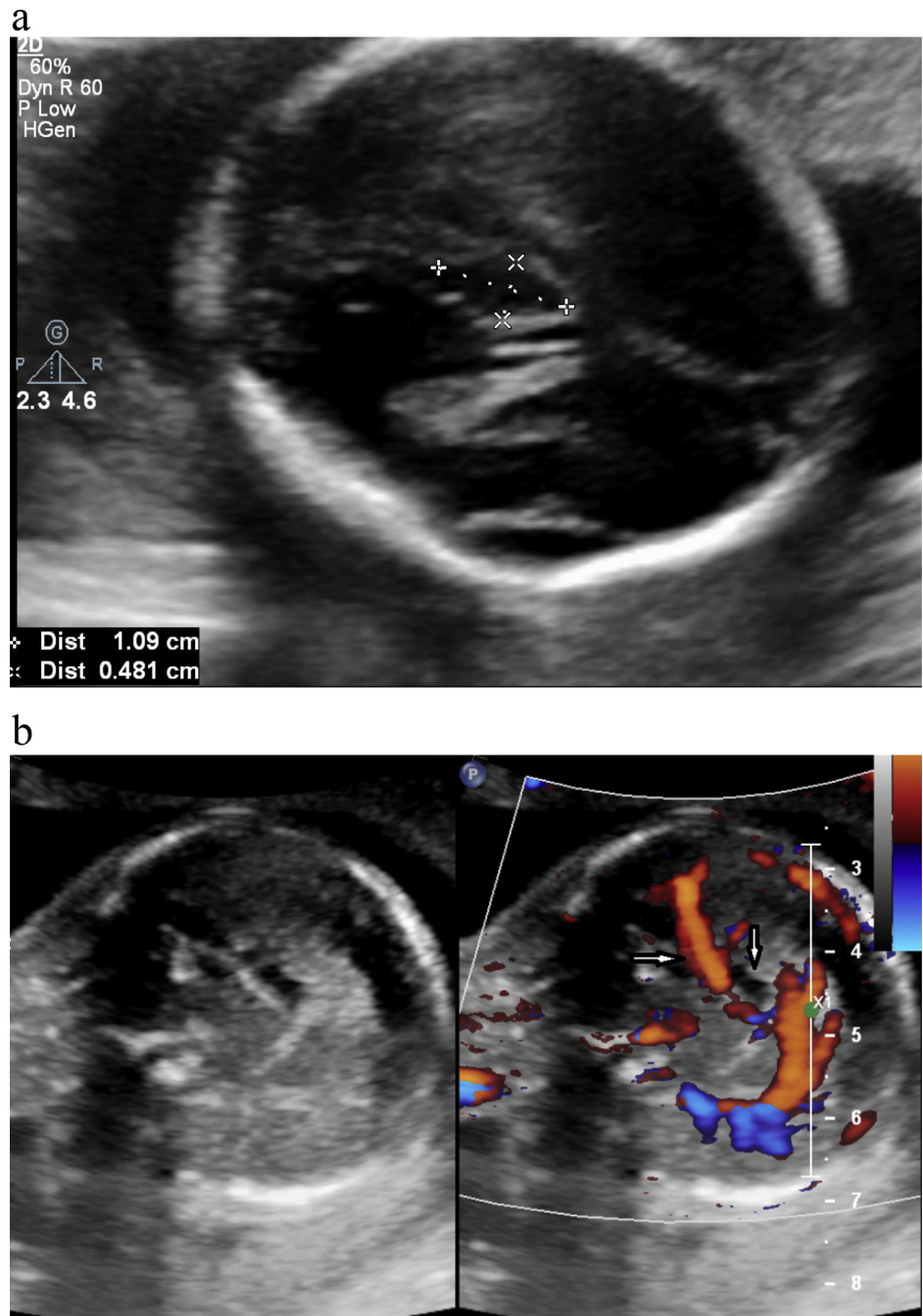


Fig. 2. A 20 weeks normal fetuses with a 10 mm Cavum veli interpositi cyst. a: The axial view shows the location of cyst in posterior and separate from cavum septum pellucidum. b: In sagittal view, Color Doppler study shows the internal cerebral vein (horizontal arrow) is located under the cyst (vertical arrow).

Table 1
Frequency of CVI cysts in normal fetuses and fetuses with CNS and extra CNS anomalies.

	With CVI cyst N (%)	Without CVI cyst N (%)	Total N
CNS anomalies	17 (23.2%)	56 (76.7%)	73
Extra-CNS anomalies	15 (18.9%)	64 (81%)	79
Normal fetuses	66 (18.3%)	294 (81.6%)	360

progressive enlargement of this cistern or it represents an abnormal separation of the crura of the fornices. These cysts are usually located superior or medial to the internal cerebral veins and

using color Doppler is useful to differentiate these cysts from a true cystic lesion of this region (arachnoid and pineal cysts) which are located down these veins [1].

It is a common finding in postnatal life, especially in infancy. In one study by pneumoencephalogram in infancy period, the incidence of CVI cysts was 34% with no gender predilection [8]. Also in another study in preterm infants, its incidence was 21% [1]. After infancy, its incidence was reported lower, for example in one study was about 5.5% [9].

However it has been rarely reported in prenatal life, only as a case report or case series and in one systematic review in 2016, only 23 cases in the fetal period were found in the literature [3,4,7,10].

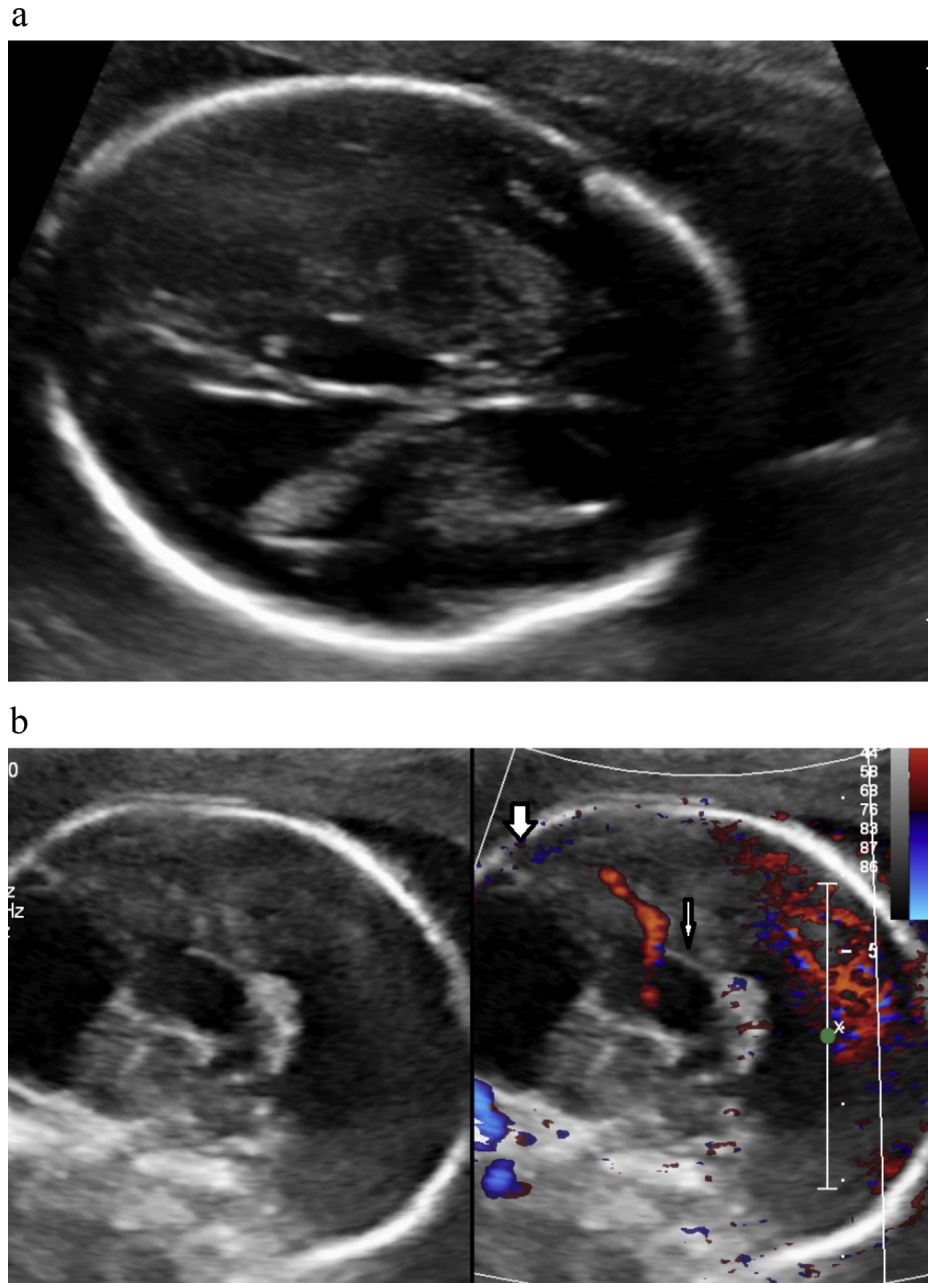


Fig. 3. A 19 weeks fetus referred for Dandy-Walker malformation. a: The axial view shows a CVI cysts and ventriculomegaly. b: In sagittal view the cyst is located above the internal cerebral vein (narrow vertical arrow). Wide vertical arrow: Dandy- Walker malformation.

Table 2

CNS anomalies in two groups of fetuses with and without CVI cyst.

CNS anomalies	Without CVI cysts		With CVI cysts	
	Percent	Number	Percent	Number
Arnold-chiari, malformation	14.1	11	16.6	3
Dandy-walker malformation	5.1	4	16.6	3
Microcephaly	2.5	2	5.5	1
Cerebellum hypoplasia	8.9	7	5.5	1
Vermian hypoplasia	10.2	8	11.1	2
Black's pouch cyst	11.5	9	22.2	4
Corpus callosum abnormality	10.2	8	11.1	2
ventriculomegaly	34.6	27	5.5	1
Cephalocele	2.5	2	5.5	1
Total	100	78	100	18

Table 3

Extra-CNS Anomalies in two groups of fetuses with and without CVI cysts.

Extra-CNS Anomaly	Without CVI cysts		With CVI cysts	
	Percent	Number	Percent	Number
Heart	28.5	52	26.9	14
Thorax	11.5	21	11.5	6
Skeleton	17	31	17.3	9
Abdomen	22.5	41	23	12
Face	9.3	17	7.6	4
Spine	10.9	20	13.4	7
Total	100	182	100	52

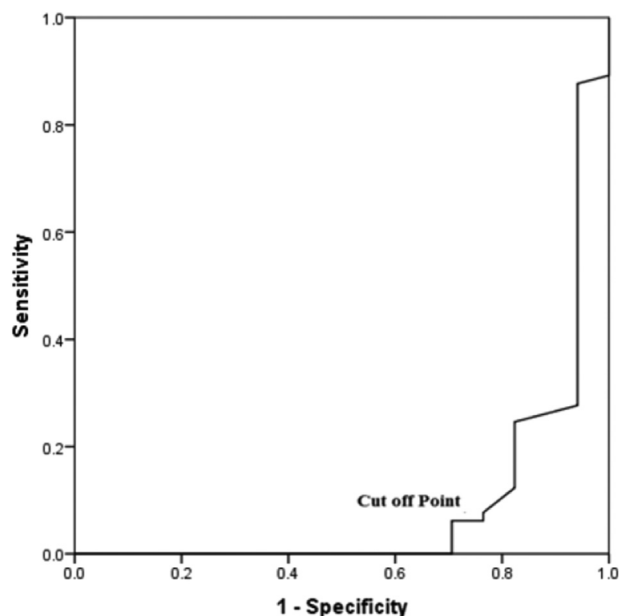


Fig. 4. ROC curve related to the cut-off point value of CVI cyst.

In this study, we found that the prevalence of these cysts in a second trimester is 18–23% and is nearly similar to its prevalence in infancy. Maybe the most important reason for this significant higher percentage in prenatal life in our study compared with previous prenatal researches is that we found and reported much smaller cysts. The mean size of cyst in normal fetuses was 4.6 mm (up to 9 mm) and only 3 cases were larger than 7.1 mm (our cut-off) in this group. But according to previous researches, most of the previously reported cysts in antenatal life were more than 8–10 mm. In one study by D'Addario et al., in 2009, the mean diameter of cysts in prenatal life was 12.4 mm (9–20 mm) [3]. Vergani et al., in 1998 had reported the mean size of physiologic cysts (cavum septi pellucidi, cavum vergae and CVI) as 10 mm (10–30 mm) [6]. Eisenberge et al., in 2003, reported two cases of second trimester CVI cysts of 6 and 8 mm [4]. Two cases also were reported by Shah et al., in 2005 with maximum diameter of cyst of 32 and 35 mm [10]. The average size of the cyst in one postnatal study was 5.6 mm (3–10 mm) almost similar to our results [1].

In this study, the cysts were larger (mean of 9.2 mm, 3.3–16 mm) and more common (23% vs 18%) in fetuses with CNS anomalies compared to normal fetuses and fetuses with extra-CNS anomalies. Also, we proposed a cut-off of cyst size of 7.1 mm in second trimester with high sensitivity, specificity, and accuracy as an alarming sign for the associated brain anomalies in the second trimester anomaly scan which needs more attention. No significant difference was found between the mean size and prevalence of cyst in normal fetuses and fetuses with extra-CNS anomalies.

There was no significant difference between the type of extra-CNS anomaly in fetuses with and without CVI cysts and cardiovascular and abdominal related anomalies were most common like as previous research results [11]. But the most common brain anomalies were different between them and were Dandy-Walker spectrum (49.9%) and then Arnold-Chiari malformation (16.6%) in fetuses with cyst, and in other group ventriculomegaly (34.6%) and then Dandy-Walker spectrum (26.8%). It is not clear why the ventriculomegaly is less common in our fetuses with cyst which is different from previous researches. One reason maybe the different sample size in this group. In a systematic review in 2016 in cases with prenatally detected cysts, the incidence of associated CNS

anomalies and extra-CNS anomalies was 31% and 6%, respectively. Also, they found Ventriculomegaly was the most common CNS anomaly [7].

The clinical significance of CVI cyst is unclear. In some recent papers, it has been reported when isolated, there were no postnatally detected associated anomalies and have not been shown to be related to abnormal clinical consequence [3,4,7]. In 17% of cases in the utero progression of cysts size occurred while the in utero regression was about 23%. Prenatally detected isolated arachnoid cyst was more likely to result in symptoms or having surgery [7,12]. Also, it has been reported in association with mental and motor development retardation, headache epilepsy, and infantile autism [13–18]. Especially large cysts and those progress in utero, can result in hydrocephalus need postnatal intervention [5,19,20]. In our study we followed 60% of our normal fetuses (isolated ones) and all of them resolved during or after birth without any complication. However, 92% (37) of our followed isolated cases were small and less than 7.1 mm (our cut-off).

In conclusion, we found CVI cysts are more common in prenatal life unlike previous results especially in fetuses with brain anomaly and it seems reasonable after prenatal diagnosis of larger cysts (>7.1 mm), the pregnancy should be evaluated for associated findings or followed for changes in cyst size or appearance of hydrocephalus. Isolated small cysts usually have a favorable outcome.

Conflict of interest

The authors declare that there are no conflict of interest.

Acknowledgements

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