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## ORIGINAL ARTICLE

# Role of Retrochorionic Blood Flow Doppler in Early Prediction of First Trimester Miscarriage

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### Abstract

*Aim/Objective:* To assess the role of retrochorionic blood flow doppler in early prediction of first trimester miscarriage.

*Background:* Miscarriage is one of the most typical early pregnancy complications and remains a significant clinical problem even today. The etiology of this condition is poorly understood, and as a result, therapy regimens are based on scant evidence.

*Methods:* This prospective cohort study was carried out at a major medical center at the Department of Obstetrics and Gynecology at Al Sayed Galal University Hospital from June 2022 till March 2023 and performed on a total of 100 patients, who presented with singleton pregnancy and gestational age from 6 to 10 weeks.

*Results:* Our results showed that clear and distinct differences emerged between the studied population regarding pulsatility index, resistance index, and systolic/diastolic ratio according to abortion. Also, there were significant differences in resistance index regarding the correlation between the week of abortion and spiral arterioles Doppler ultrasound findings and diagnostic performance of spiral arterioles Doppler ultrasound findings in predicting abortion.

*Conclusion:* We concluded that in early pregnancy (between 6 and 8 weeks), spiral artery Doppler analysis may provide a noninvasive indicator of insufficient trophoblast invasion as a screening test for early prediction of miscarriage.

*Keywords:* First trimester, Miscarriage, Retrochorionic blood flow Doppler

## 1. Introduction

Spontaneous abortion, commonly referred to as miscarriage, is characterized by the termination of pregnancy occurring before the completion of 20 gestational weeks. In accordance with the American College of Obstetricians and Gynecologists (ACOG), it is estimated that this particular type of pregnancy loss is the most prevalent. According to estimates, approximately miscarriage occurs in 26% of pregnancies, including as many as 10% of confirmed pregnancies being affected.<sup>1</sup> In addition, the first trimester accounts for 80% of all early pregnancy losses. After 12 weeks of pregnancy, the risk of miscarriage reduces.<sup>2</sup>

Since the risk of miscarriage is complex, with some maternal risk factors appearing to be more important than others, there is no single predictor of

future pregnancy loss. The age of the mother is a major factor in determining the probability of a miscarriage. The chance of miscarriage in women aged 20–30 years is 8.9% before 20 weeks of pregnancy. The percentage rises to 74.7% for women over the age of 40 years.<sup>3</sup>

There is an increased chance of miscarriage when the mother has certain comorbid conditions, for instance, thrombophilia, antiphospholipid antibody syndrome, excessive maternal weight, and hypertension. Cigarette smoking, caffeine use over recommended levels, trauma, and maternal malnutrition are additional risk factors found.<sup>4</sup>

Transvaginal color Doppler spiral sonography has allowed for an improved understanding of circulation between the uterus and the placenta during the first trimester. Researchers were motivated to try to detect obstetrical challenges throughout pregnancy

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associated to aberrant placentation using Doppler sonography that allows for the monitoring of blood flow throughout the uteroplacental circulation, including its most distal branches.<sup>5</sup>

Uteroplacental circulation is a complex system in which the volume of blood flow through an individual vessel can vary considerably. As a result, assessing blood flow in specific uteroplacental vessels can be challenging and provides limited insight into the underlying mechanisms of placental disorders during pregnancy.<sup>6</sup>

Doppler ultrasound is widely used for non-invasively measuring blood flow impedance for several decades now. Multiple studies have reported using the rate of blood flow change in the uterine artery (UA) to evaluate uteroplacental circulation in the first trimester of pregnancy; however, the results seem to be at odds with one another.<sup>4</sup>

It is of interest to determine if aberrant patterns of blood flow in the spiral artery precede miscarriage and if they represent vascular remodeling in the maternal–fetal interface during placentation. Because of this, researchers decided to use ultra-sensitive Doppler indices to analyze the alterations in blood flow impedance of the UA and the spiral artery throughout the first trimester of pregnancy.<sup>5</sup>

The study's primary objective was to assess the role of retrochorionic blood flow Doppler in early prediction of first trimester miscarriage.

## 2. Patients and methods

One hundred women in their first trimester of pregnancy participated in this prospective cohort research. They were seeking prenatal care and

agreed to participate after receiving clearance from an ethics committee and providing informed consent. The study was conducted at the Department of Obstetrics and Gynecology at Al Sayed Galal University Hospital, Al-Azhar University from June 2022 to March 2023.

**Methodology:** Doppler study was conducted on 100 pregnant women coming for antenatal care with gestational ages ranging between 6 and 10 weeks. Results were registered and the patients were followed up till 12 weeks to determine who completed their first trimester without complications and who experienced miscarriage, either missed or spontaneous.

### 2.1. Inclusion criteria

Age range: 18–35 years, 6–10 week gestational age, and singleton pregnancy.

### 2.2. Exclusion criteria

Age below 18 years or greater than 35 years, gestational age greater than 12 weeks, multiple uterine pregnancy, history of diabetes mellitus, and/or hypertension, history of uterine malformation, history of autoimmune diseases, and history of coagulation disorders.

#### 2.2.1. Study procedure

All patients underwent: full detailed history, complete examination, investigations, and imaging assessment.

Sample size: 100.

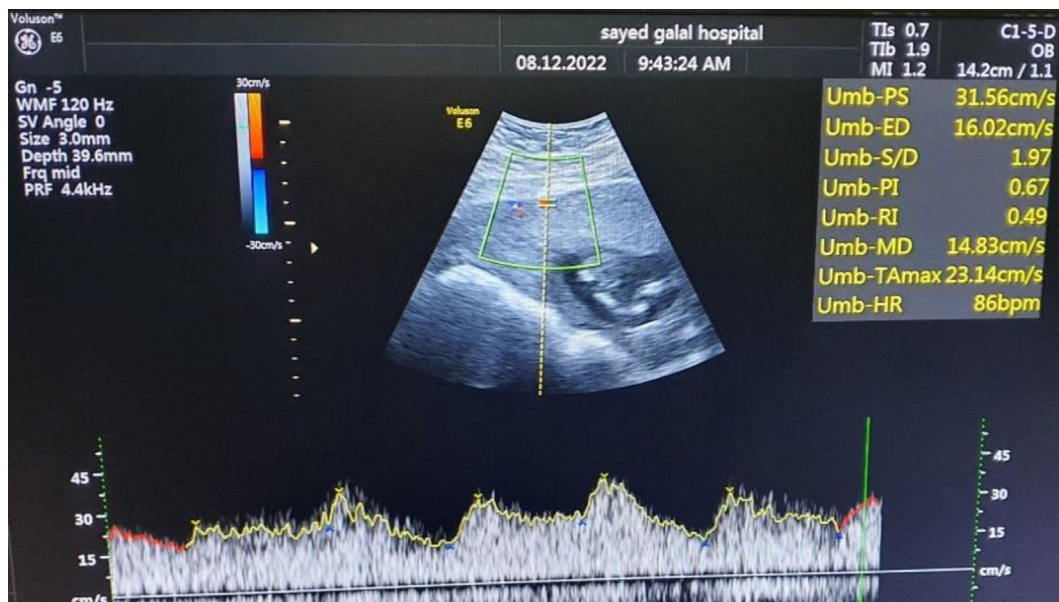


Fig. 1. Systolic/diastolic (S/D) ratio.

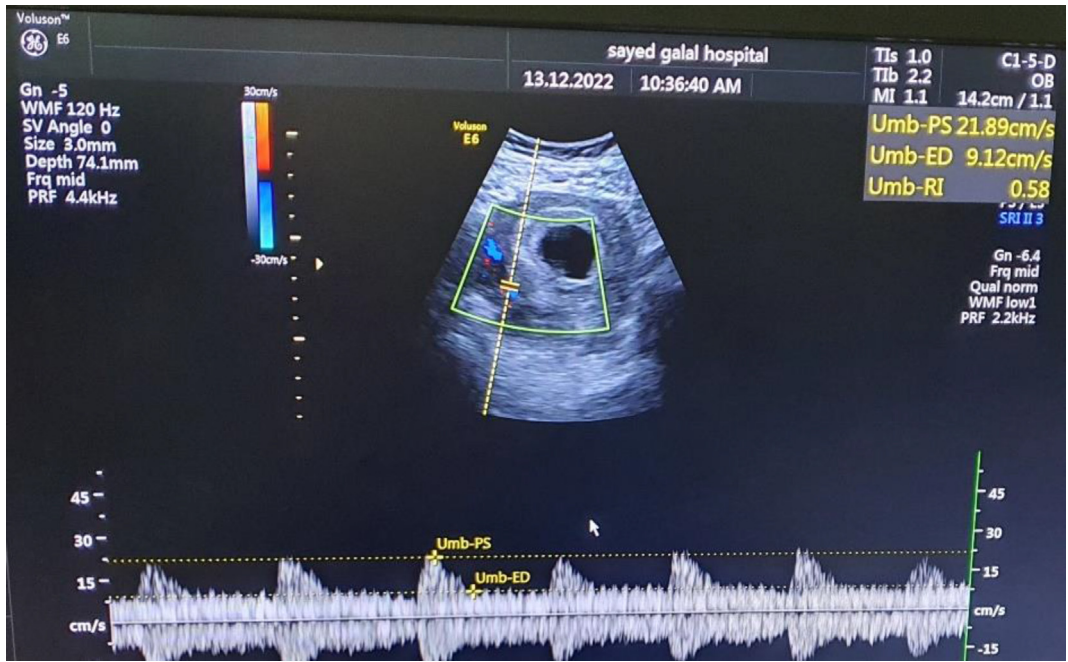


Fig. 2. Resistance index (RI).

2.3. Ultrasound/Doppler evaluation

The same physician used a real-time, 6.0 MHz endo-vaginal probe attached to a (Voluson E6) for the sonograms. Each sonographic procedure was carried out by the same researcher so that no differences may have resulted from different observers. Approximately 5–10 min were spent on each test (ultrasound and Doppler).

2.4. Primary outcome

First trimester miscarriage.  
There was no secondary outcome.

2.5. Outcome measures

Correlation between Doppler changes and adverse pregnancy outcomes: when measuring

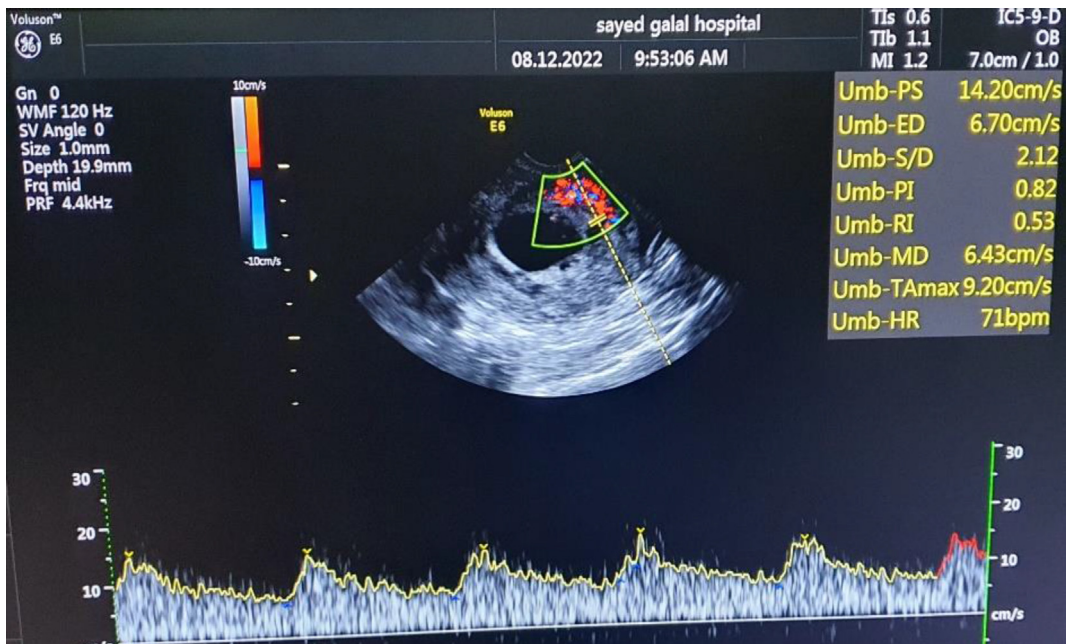


Fig. 3. Pulsatility index (PI).



Table 1. Comparative demographics of the sample population.

Variables	Mean $\pm$ SD	Range
Age (years)	26.5 $\pm$ 3.7	18.0–35.0
BMI (kg/m <sup>2</sup> )	29.7 $\pm$ 2.2	23.4–34.8
GA (weeks)	7.0 $\pm$ 1.5	6.0–8.0
Parity	<i>n</i> (%)	
Nulli	38 (38.0)	
Parous	62 (62.0)	

Total = 100.

GA, gestational age.

Table 2. Spiral arterioles Doppler ultrasound findings among the studied cases.

Doppler items	Mean $\pm$ SD	Range
Pulsatility index	0.94 $\pm$ 0.22	0.43–1.61
Resistive index	0.46 $\pm$ 0.07	0.34–0.65
Systolic/diastolic ratio	2.18 $\pm$ 0.29	1.64–2.84

Total = 100.

blood flow through the body's spiral arteries, researchers will take the mean of the values measured from two successive flow velocity waveforms. These metrics were determined (Figs. 1–3).

### 2.6. Ethical consideration

Data collection was developed on considerations of ethics. The study protocol obtained ethical approval from the Faculty of Medicine's ethical council at Al-Azhar University. Written consent with explanations was obtained from all participants women, ensuring confidentiality and privacy to the personal data of the participant women.

### 2.7. Statistical analysis

The data that was gathered underwent coding, tabulation, and statistical analysis using IBM SPSS Statistics software, version 22.0, developed by IBM

Corp. (Chicago, Illinois, USA in 2013). In addition, Microsoft Office Excel 2007 was used in the analysis process.

Quantitative data was described using mean  $\pm$  SD and lowest and highest of the range, whereas counts and percentages were used to provide a description of the qualitative data.

Inferential analysis was performed on quantitative variables with the help of the Shapiro–Wilk test for normality, and the independent *t*-test was used when comparing two different groups that had normally distributed data. In qualitative data with very few predicted numbers, the  $\chi^2$  test was used to make comparisons of proportions, whereas Fisher's exact test was used to make comparisons of means for independent variables. The cutoff for statistical significance was set at a *P* value of 0.050.

## 3. Results

Table 1 shows that the mean  $\pm$  SD of age was 26.5  $\pm$  3.7 years, of BMI was 29.7  $\pm$  2.2 kg/m<sup>2</sup>, and of gestational age at enrollment was 7.0  $\pm$  1.5 weeks. About 38% of the women in the samples did not have any live births.

Table 2 shows that Doppler ultrasound evidence of spiral arteries in the instances analyzed. Mean  $\pm$  SD of pulsatility index (PI), resistive index (RI), and systolic/diastolic (S/D) ratio was 0.94  $\pm$  0.22, 0.46  $\pm$  0.07, and 2.18  $\pm$  0.29, respectively (Table 3).

Table 4. Correlation between week of abortion and spiral arterioles Doppler ultrasound findings.

Doppler findings	<i>r</i> (correlation coefficient)	<i>P</i> value
Pulsatility index	–0.188	0.441
Resistive index	–0.694	0.001 <sup>a</sup>
Systolic/diastolic ratio	–0.113	0.645

Pearson correlation test.

<sup>a</sup> Significant.

Table 3. Contrast in terms of abortion.

Variables	Aborted ( <i>N</i> = 19)	Continued ( <i>N</i> = 81)	<i>P</i> value
Age (years)	25.3 $\pm$ 4.5	26.8 $\pm$ 3.5	0.125 <sup>a</sup>
BMI (kg/m <sup>2</sup> )	30.3 $\pm$ 1.9	29.6 $\pm$ 2.2	0.182 <sup>a</sup>
GA (weeks)	9.32 $\pm$ 1.1	8.9 $\pm$ 1.4	0.280 <sup>a</sup>
Parity [ <i>n</i> (%)]			
Nulli	7 (36.8)	31 (38.3)	
Parous	12 (63.2)	50 (61.7)	0.908 <sup>b</sup>
Pulsatility index	1.06 $\pm$ 0.23	0.88 $\pm$ 0.23	0.002 <sup>c,a</sup>
Resistive index	0.55 $\pm$ 0.07	0.44 $\pm$ 0.05	<0.001 <sup>c,a</sup>
Systolic/diastolic ratio	2.38 $\pm$ 0.26	2.13 $\pm$ 0.28	<0.001 <sup>c,a</sup>

<sup>a</sup> Independent *t*-test.<sup>b</sup>  $\chi^2$  test.<sup>c</sup> Significant.

Table 5. Diagnostic capability of spiral arterioles Doppler ultrasound findings in predicting abortion.

Doppler findings	AUC	SE	P value	95% CI	Cut point
Pulsatility index	0.693	0.064	0.009 <sup>a</sup>	0.568–0.819	≥0.97
Resistive index	0.879	0.052	<0.001 <sup>a</sup>	0.777–0.981	≥0.49
Systolic/diastolic ratio	0.735	0.064	0.001 <sup>a</sup>	0.610–0.860	≥2.25

AUC, area under curve; CI, confidence interval.

<sup>a</sup> Significant.

Table 6. Diagnostic characteristics of spiral arterioles Doppler ultrasound cut points in predicting abortion.

Characters	Pulsatility index ≥0.97 (%)		Resistive index ≥0.49 (%)		Systolic/diastolic ratio ≥2.25 (%)
Sensitivity	68.4	43.4–87.4	78.9	54.4–93.9	73.7
Specificity	56.8	45.3–67.8	90.1	81.5–95.6	65.4
DA	59.0	48.7–68.7	88.0	80.0–93.6	67.0
YI	25.2	1.7–48.7	69.1	49.6–88.5	39.1
PPV	27.1	15.3–41.8	65.2	42.7–83.6	33.3
NPV	88.5	76.6–95.6	94.8	87.2–98.6	91.4
LR+	1.58	1.07–2.35	7.99	3.98–16.06	2.13
LR–	0.56	0.28–1.11	0.23	0.10–0.56	0.40
DOR	2.85	0.98–8.24	34.22	9.12–128.43	5.30

DA, diagnostic accuracy; NPV, negative predictive value; PPV, positive predictive value; YI, Youden's index.

Positive likelihood ratio, LR: negative likelihood ratio, LR: diagnostic odds ratio.

There were no statistically significant differences between aborted and nonaborted cases with respect to age, BMI, gestational age, or number of children, but there were statistically greater values for the PI, the resistive index, and the S/D ratio.

Table 4 showed that only the resistive index had a statistically significant correlation with the week of abortion.

Table 5 shows that abortion could be predicted with a considerable moderate diagnostic performance using the resistive index, while PI and S/D ratio statistically had significant low diagnostic performance.

Table 6 shows that RI more than or equal to 0.49 had the highest predictive value for abortion identified; it had high specificity and negative predictive value but low other characteristics.

#### 4. Discussion

Patients who present with vaginal bleeding have a three to four times increased chance of miscarriage compared with the control population. Twenty percent to twenty-five percent of women who are early in their pregnancies may present with a detected threatening miscarriage that lasts for days or weeks.<sup>1</sup> The placenta is the most common source of early pregnancy hemorrhage. It can have both immediate and far-reaching consequences for the progress of the pregnancy and its outcome.<sup>5</sup>

The findings of the present investigation indicate that the average age was  $26.5 \pm 3.7$  years, while BMI was  $29.7 \pm 2.2$  kg/m<sup>2</sup>. Gestational mean age at enrolment was  $7.0 \pm 1.5$  weeks and 38.0% of the

studied cases were nulliparous. Abortion occurred in 19.0% of the studied cases, while 81% of cases continued pregnancy.

No statistically significant variations in age, BMI, gestational age, or parity were found between abortion groups ( $P = 0.125, 0.182, 0.280,$  and  $0.908,$  respectively).

As regards Doppler ultrasound findings, the current study results showed that PI, RI and S/D ratio were statistically significantly higher in aborted cases ( $P > 0.001$ ), while only the resistive index had a statistically significant correlation with the weeks of abortion ( $P = 0.001$ ).

These findings corroborate those of previous research by Bhoil et al.,<sup>5</sup> who conducted a cross-sectional study that enrolled 50 pregnant females for evaluation and comparison of spiral artery flow between threatening abortion and normal pregnancies during the first trimester, namely between weeks 4 and 8 and revealed significant differences in the spiral artery Doppler values of RI and PI in the two groups, which are higher in abortion cases ( $P = 0.003, 0.041,$  respectively). Nonetheless, the S/D levels did not differ significantly between the two groups ( $P = 0.147$ ).

The findings of this study align with the results reported by Sharma and colleagues in their prospective study, which involved the enrollment of 100 patients. Using extremely sensitive Doppler indices, Sharma and colleagues set out to examine changes in UA blood flow impedance throughout early pregnancy. Their study revealed that during the first trimester of pregnancy, there were noticeable shifts

in the UA's resistance to blood flow. The research demonstrated instances of spontaneous abortion accompanied by impaired growth of the gestational sac. In these cases, however, during weeks 5 and 6, the UA-RIs either remained elevated ( $RI > 0.8$ ) or did not decline as predicted. Furthermore, vascular resistive indices were found to be higher in the group that experienced subsequent miscarriage compared with those who had continuing pregnancies.<sup>7</sup>

The elevated UA-RI observed during the 5th and 6th week of pregnancy could potentially contribute to spontaneous abortion. This increase in UA-RI may indicate compromised vascular remodeling, which can be attributed to the inadequate invasion of trophoblasts during placentation.<sup>8</sup>

Later on, similar findings were reported by other investigators, Jing, who conducted a retrospective study that included 60 pregnant women with threatened abortion in early pregnancy to investigate the potential value of transvaginal color Doppler ultrasonography in the early pregnancy differential identification of abortion-threatening conditions and found that the uterine spiral artery PI and luteal blood flow RI were both considerably greater in the abortion group than in the control group.<sup>9</sup>

This study aligns with prior research conducted by Ozkaya and colleagues, in which uteroplacental circulation in a group of 105 pregnant women was studied using Doppler sonography between weeks 6 and 12. The objective of the study was to investigate whether spectral Doppler measurements obtained from bilateral uterine, arcuate, radial, and spiral arteries during early gestation are associated with adverse pregnancy outcomes. The findings showed that higher PI and RI values were found in the UAs of women who had poor obstetric outcomes compared with women who had normal PI and RI values.<sup>10</sup>

As regards diagnostic performance of Doppler ultrasound findings in predicting abortion, the current study results showed that the RI showed a noteworthy moderate level of diagnostic efficacy in its ability to predict abortion, whereas PI and S/D ratio statistically had significant low diagnostic performance. RI more than or equal to 0.49 had highest diagnostic characteristics in predicting abortion with a negative predictive value of 94.8% and a high degree of specificity of 90.1%, but low other characteristics.

To obtain accurate diagnostic data while staying in accordance with local, state, and federal laws, it is crucial to use control settings that minimize thermal and mechanical indices as much as possible.<sup>11</sup>

Furthermore, ultrasound exposure should be minimized in accordance with the 'as low as reasonably achievable' (ALARA) approach. In our investigation, ultrasonographic examination procedures were conducted using a mechanical index of 0.82 and a thermal index for soft tissues (TIs) of 0.7. The British Medical Ultrasound Society Guidelines Ter Haar served as the basis for the selection of these values<sup>12</sup> in order to prevent harm when using ultrasonography for medical diagnosis. In addition, patients whose examination could not be finished in less than 10 min were omitted from the current study to prevent unnecessary exposure to radiation.

The screen test demonstrates a notable negative predictive value, indicating that a normal Doppler result provides a high level of confidence in predicting a favorable outcome.<sup>7</sup>

It is important to acknowledge the limitations of the study, one of which is the absence of inclusion or exclusion criteria for an embryonic pregnancies. The present study was carried out at a singular research facility, which limited the scope of the target group and thereby diminished the generalizability of the findings to a broader patient population, thus compromising the study's external validity. Technical difficulties arise when using pulsed Doppler ultrasonography on narrow channels like spiral arteries, and the technique is highly dependent on the skill of the sonographer, therefore it is important to keep that in mind. This may be a barrier to its widespread implementation in everyday clinical practice.

#### 4.1. Conclusion

As evident from the current study, Doppler examination of spiral arteries during the first few weeks of pregnancy may be a helpful, noninvasive evaluation for the screening of reduced trophoblast invasion and early prediction of miscarriage.

#### Conflict of interest

There are no conflicts of interest.

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