

Retrospective Study

Gastric polyps: Association with *Helicobacter pylori* status and the pathology of the surrounding mucosa, a cross sectional study

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Abstract

AIM: To assess the endoscopic characteristics of gastric polyps and their association with *Helicobacter pylori* (*H. pylori*) status in a predominantly Hispanic population.

METHODS: We conducted a retrospective study of all esophagogastroduodenoscopies performed at our institution. Demographic, endoscopic and histopathological data were reviewed. Categorization of patients into Hispanic and Non-Hispanic was based on self-identification. Patients without resection/biopsy were not included in the analysis. Identification of polyps type was based on histological examination. One way analysis of variance was used to compare continuous

variables among different polyp types and Fisher's exact test was used compare categorical variables among polyp types. Unadjusted and adjusted comparisons of demographic and clinical characteristics were performed according to the *H. pylori* status and polyp type using logistic regressions.

RESULTS: Of 7090 patients who had upper endoscopy, 335 patients had gastric polyps (4.7%). Resection or biopsy of gastric polyps was performed in 296 patients (88.4%) with a total of 442 polyps removed or biopsied. Of 296 patients, 87 (29%) had hyperplastic polyps, 82 (28%) had fundic gland polyps and 5 (1.7%) had adenomatous polyps. Hyperplastic polyps were significantly associated with positive *H. pylori* status compared with fundic gland polyps (OR = 4.621; 95%CI: 1.92-11.13, $P = 0.001$). Hyperplastic polyps were also found to be significantly associated with portal hypertensive gastropathy compared with fundic gland polyps (OR = 6.903; 95%CI: 1.41-33.93, $P = 0.0174$). Out of 296 patients, 30 (10.1%) had a follow-up endoscopy with a mean duration of 26 ± 16.3 mo. Interval development of cancer was not noted in any of the patients during follow up period.

CONCLUSION: Gastric hyperplastic polyps were significantly associated with positive *H. pylori* status and portal hypertensive gastropathy as compared with fundic gland polyps.

Key words: Gastric polyps; Fundic gland polyp; Hyperplastic polyp; Adenomatous polyps; Chronic gastritis; *Helicobacter pylori*

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Core tip: In a predominantly Hispanic population, the most common gastric polyps were hyperplastic and fundic gland polyps (more than half of gastric polyps). Gastric hyperplastic polyps were significantly associated with positive *Helicobacter pylori* status and portal hypertensive gastropathy as compared with fundic gland polyps. Hyperplastic polyps and fundic gland polyps were more prevalent in chronic gastritis, while adenomatous polyps were associated with intestinal metaplasia.

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INTRODUCTION

Gastric polyps can be defined as abnormal luminal growths projecting above the plane of the mucosal

surface. The incidence of gastric polyps has been estimated to be between 2% and 6%. The incidence of gastric polyps is gradually increasing due to expanded indications and widespread use of endoscopic examinations^[1-4]. Gastric polyps are usually asymptomatic and discovered incidentally during endoscopic examination, but on rare occasions they can present with nonspecific symptoms such as abdominal pain, gastrointestinal bleeding, anemia, or symptoms of gastric outlet obstruction^[5-8]. Determination of gastric polyp type is important as the risk for malignant transformation depends on the histopathological nature of the polyp^[9-12]. The frequency of different types of gastric polyps varies widely depending on the population studied. It has been reported that hyperplastic polyps are relatively more frequent than fundic gland polyps in regions where *Helicobacter pylori* (*H. pylori*) infection is common^[1,13]. A higher prevalence of *H. pylori* infection has been documented in Hispanics living in United States regions bordering Mexico compared with non-border areas^[14,15]. There is a paucity of published data from the United States regarding the nature and various characteristics of gastric polyps, especially in Hispanics and other immigrant groups. The aim of this study is to assess the prevalence of gastric polyps and their endoscopic and histological characteristics in a predominantly Hispanic population on the United States-Mexico border.

MATERIALS AND METHODS

Study design

After receiving approval from Texas Tech University Institutional Review Board, we retrospectively reviewed all esophagogastroduodenoscopies (EGDs) performed at the University Medical Center, El Paso, TX for all indications. The review period of the study was from November 1, 2007 to July 30, 2013. The electronic database system (ProVation®, Minneapolis, MN) was used to identify the patient's demographic data, the indication for the procedure and gastric polyp characteristics. Categorization of patients into Hispanic and Non-Hispanic was based on self-identification. Patients without resection/biopsy were not included in the analysis. Identification of polyps type was based on histological examination.

Statistical analysis

Quantitative variables were described using the mean \pm SD, whereas categorical variables were described using the frequency and proportion. One way analysis of variance was used to compare continuous variables among different polyp types and Fisher's exact test was used compare categorical variables among polyp types. Unadjusted and adjusted comparisons of demographic and clinical characteristics were performed according to the *H. pylori* status and polyp type using logistic regressions. The logistic regression analysis for *H. pylori* status was conducted after removing *H. pylori*

Table 1 Patient level summary of polyp histology

Polyp's type	Total patients (n = 296)	Percentage
Hyperplastic polyp	87	29.39
Fundic gland polyp	82	27.7
Chronic gastritis	41	13.85
Mixed	13	4.39
Intestinal metaplasia	12	4.05
Foveolar hyperplasia	10	3.38
Adenoma	5	1.69
Carcinoid tumor	4	1.35
Granulation tissue polyp	4	1.35
Adenocarcinoma	2	0.68
Gastric xanthelasma	2	0.68
Hamartomatous polyp	2	0.68
Lymphoid follicles	2	0.68
Submucosal Brunner glands	2	0.68
Lipoma	1	0.34
Normal	27	9.12

not tested patients. The logistic regression was used to find out factors associated with hyperplastic polyp type as compared with fundic polyp type after removing patients with adenoma, mixed polyps, and others. The results of logistic regression analysis were reported using odds ratio (OR), 95%CI and *P* values. Stepwise selection method using probability to enter = 0.10 and probability to stay = 0.05 was used to obtain the final model. All the statistical analyses were carried out using statistical analysis software (SAS) 9.3. Results were considered significant at the 5% level of significance. The statistical methods of this study were reviewed by Dr. Alok Dwivedi from the department of Biostatistics at Texas Tech University HSC at El Paso.

RESULTS

Demographic and clinical characteristics

A total of 7090 patients underwent 9450 EGD procedures. Of these, 335 patients had gastric polyps (4.7%). Resection or biopsy of 442 gastric polyps was done in 296 patients (88.4%). 39 patients did not undergo resection or biopsy of their gastric polyps because of the high risk of bleeding or obvious endoscopic diagnosis of fundic gland polyps (FGPs). The mean age of the patients was 58 years (SD: \pm 12 years). The majority of the patients were females (74%) and most were Hispanics (85%). Portal hypertensive gastropathy was seen in 20 patients (7%).

Endoscopic and histopathological features

Polyps' histology: Of 296 patients, 87 (29%) patients had hyperplastic polyps and 82 (28%) patients had fundic gland polyps. There were 5 (1.7%) patients with adenomatous polyps while 13 (4.4%) patients had mixed types of polyps. Histology results of the remaining polyps revealed chronic gastritis in 41 patients (14%), intestinal metaplasia in 12 patients (4.1%), foveolar hyperplasia in 10 patients (3.4%), carcinoid tumor in 4 patients (1.4%) and granulation

tissue polyps in 4 patients (1.4%). Adenocarcinoma, gastric xanthelasma, hamartomatous polyps, lymphoid follicles and submucosal brunner glands were each found in 2 patients (0.68%). There was one patient with lipoma. The histology of resected or biopsied polyp was normal in 27 patients (9.1%).

Pathology of the surrounding mucosa: Out of 296 patients, 266 (89.8%) patients had biopsies of the surrounding mucosa (Table 1).

Of these, 190 (64%) patients had chronic gastritis while 25 (8%) patients had intestinal metaplasia. Thirty (10%) patients were not biopsied. In regards to *H. pylori* status, *H. pylori* were positive in 71 (24%) patients, and negative in 211 (71%) patients, while 14 patients were not tested.

Clinical characteristics of gastric polyps: Table 2 shows the distribution of patient and clinical characteristics according to five categories (Adenoma, Hyperplastic, Fundic gland, Mixed and other) of polyps. The gender and ethnicity distributions were not found to be significantly different among different polyp types. The distribution of age, pathology of surrounding gastric mucosa, and *H. pylori* status were found to be associated with different polyp types. Adenomatous polyps were more common in advanced age ($P < 0.0013$). Fundic, hyperplastic and mixed polyps were more frequent in chronic gastritis while adenomatous polyps were more common (60%) in intestinal metaplasia ($P < 0.001$). Thirty-one percent of the patients with hyperplastic polyps tested positive for *H. pylori* status while 9.8% of the patients with fundic gland polyps tested positive for *H. pylori*. Portal hypertensive gastropathy was seen in 11.5% of patients with hyperplastic polyps compared to 2.4% of patients with fundic gland polyps.

Associations of *H. pylori* status and gastric pathology: The prevalence of hyperplastic polyps was 34% in the *H. pylori* positive group while the prevalence of fundic polyps was 10% in the *H. pylori* positive group. Table 3 shows the unadjusted and adjusted associations of cofactors with *H. pylori* status. Only the polyp type and the pathology of surrounding gastric mucosa were associated with *H. pylori* in unadjusted and adjusted models. Hyperplastic polyps have a 4.6 times higher odds of having a positive *H. pylori* status compared to fundic gland polyps (OR = 4.621; 95%CI: 1.92-11.13, $P = 0.001$).

Cofactors association of hyperplastic and fundic gland polyps: Table 4 shows the unadjusted and adjusted associations of cofactors with hyperplastic polyps as compared with fundic polyps. In the unadjusted analysis, age, *H. pylori* status and portal hypertension were found to be associated with hyperplastic polyps. Per unit increase in age increased the odds of hyperplastic polyp type by 3% as compared

Table 2 Distribution of patient and clinical characteristics according to different polyp types *n* (%)

Cofactor	Adenoma <i>n</i> = 5	Fundic <i>n</i> = 82	Hyperplastic <i>n</i> = 87	Mixed <i>n</i> = 13	Other <i>n</i> = 109	<i>P</i> value
Age (yr), mean ± SD	75.4 (3.3)	54.7 (13.0)	58.4 (10.8)	62.2 (14.0)	57.7 (11.9)	0.0013
Gender						0.2086
Female	5 (100.0)	67 (81.71)	64 (73.56)	9 (69.23)	75 (68.81)	
Male	0 (0.00)	15 (18.29)	23 (26.44)	4 (30.77)	34 (31.19)	
Ethnicity						0.7427
Hispanic	5 (100.0)	66 (80.49)	77 (88.51)	11 (84.62)	93 (85.32)	
Non-Hispanic White	0 (0.00)	5 (6.10)	4 (4.60)	0 (0.00)	8 (7.34)	
Other	0 (0.00)	11 (13.41)	6 (6.90)	2 (15.38)	8 (7.34)	
Pathology of surrounding gastric						< 0.0001 ¹
Chronic gastritis	0 (0.00)	51 (62.20)	52 (59.77)	9 (69.23)	78 (41.05)	
Intestinal metaplasia	3 (60.00)	1 (1.22)	6 (6.90)	1 (7.69)	14 (56.00)	
Other	0 (0.00)	22 (26.83)	15 (17.24)	2 (15.38)	5 (16.67)	
Not biopsied	2 (40.00)	8 (9.76)	14 (16.09)	1 (7.69)	12 (23.53)	
<i>Helicobacter pylori</i> status						0.0006 ¹
Negative	4 (80.00)	70 (85.37)	52 (59.77)	11 (84.62)	74 (35.07)	
Positive	0 (0.00)	8 (9.76)	27 (31.03)	2 (15.38)	34 (47.89)	
Not tested	1 (20.00)	4 (4.88)	8 (9.20)	0 (0.00)	1 (7.14)	
Portal hypertensive gastropathy						0.1821
No	5 (100.0)	80 (97.56)	77 (88.51)	12 (92.31)	102 (93.58)	
Yes	0 (0.00)	2 (2.44)	10 (11.49)	1 (7.69)	7 (6.42)	

¹*P* value was obtained using χ^2 test.**Table 3** Unadjusted and adjusted associations of cofactors with *Helicobacter pylori* positive status (*n* = 262)

Cofactor	Unadjusted OR (95%CI), <i>P</i> value	Adjusted OR (95%CI), <i>P</i> value
Age (yr)	1.011 (0.988-1.034), 0.3686	
Polyp type		
Fundic (referent)	1	1
Hyperplastic	4.621 (1.918-11.133), 0.0006	4.621 (1.861-11.479), 0.0010
Other	3.469 (1.509-7.976), 0.0034	2.952 (1.250-6.972), 0.0136
Gender		
Female (referent)	1	
Male	0.891 (0.460-1.726), 0.7321	
Ethnicity		
Hispanic (referent)	1	
Non-hispanic White	0.205 (0.026-1.605), 0.1311	
Other	0.409 (0.117-1.435), 0.1629	
Pathology of surrounding gastric		
Chronic gastritis (referent)	1	1
Intestinal metaplasia	0.996 (0.407-2.437), 0.9931	0.827 (0.331-2.065), 0.6848
Other	0.088 (0.021-0.375), 0.0010	0.090 (0.021-0.390), 0.0013
Portal hypertension		
No (referent)	1	
Yes	0.569 (0.159-2.044), 0.3877	

with fundic gland polyp. After adjusting for all other factors, *H. pylori* status and portal hypertensive gastropathy were the only remained significant factors in the final adjusted model. Positive *H. pylori* status has 5.3 times higher odds to have hyperplastic polyps compared with negative *H. pylori* status (OR = 5.285;

Table 4 Unadjusted and adjusted associations of cofactors with hyperplastic polyps as compared with fundic polyps (*n* = 143)

Cofactor	Unadjusted OR (95%CI), <i>P</i> value	Adjusted OR (95%CI), <i>P</i> value
Age (yr)	1.031 (1.001-1.062), 0.0419	
<i>H. pylori</i> status		
Negative (referent)	1	1
Positive	4.622 (1.918-11.137), 0.0006	5.285 (2.166-12.892), 0.0003
Gender		
Female (referent)	1	
Male	1.804 (0.756-4.303), 0.1837	
Ethnicity		
Hispanic (referent)	1	
Non-Hispanic White	0.469 (0.083-2.655), 0.3922	
Other	0.536 (0.150-1.923), 0.3390	
Pathology of surrounding gastric		
Chronic gastritis (referent)	1	
Intestinal metaplasia	5.997 (0.697-51.614), 0.1029	
Other	0.714 (0.331-1.542), 0.3917	
Portal hypertension		
No (referent)	1	1
Yes	5.080 (1.057-24.414), 0.0424	6.903, 0.0174

95%CI: 2.17-12.89, *P* = 0.0003) after adjusting for portal hypertensive gastropathy. Patients with portal hypertensive gastropathy are 6.4 times more likely to have hyperplastic polyps after adjusting for *H. pylori*

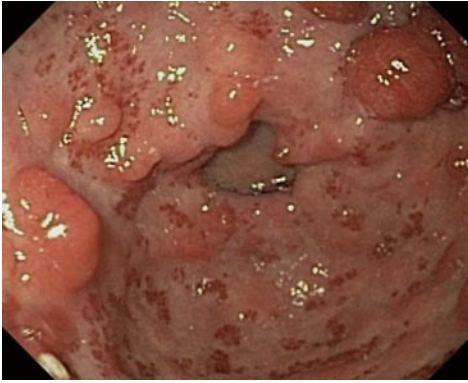


Figure 1 Multiple hyperplastic polyps in the setting of portal hypertensive gastropathy.

status (OR = 6.903; 95%CI: 1.40-33.93, $P = 0.0174$).

Long term follow-up

Out of 296 patients, 30 (10.1%) had a follow-up endoscopy with a mean duration of 26 ± 16.3 mo. Out of these 30 patients, 11 (36.6%) had hyperplastic polyps, 5 had chronic gastritis polyp, 4 had fundic gland polyp, two had intestinal metaplasia, two had carcinoid tumor, two had faveolar hyperplasia, one had adenomatous polyp and 3 patients were classified as other (gastric adenocarcinoma, brunner gland hyperplasia and normal pathology). Polyp's recurrence was noted in five out of eleven hyperplastic polyps and one out of four fundic gland polyps surveyed.

All Five adenomatous polyps were polypectomized during the initial endoscopy session. Four out of the five patients with adenomatous polyps were lost to follow-up in our system. Recurrence of the adenomatous polyp was noted in the one patient who had surveillance endoscopy.

Interval development of cancer was not noted in any of the patients during follow up period.

DISCUSSION

In this study, we found the prevalence of gastric polyps to be 4.7% in a predominantly Hispanic population, which is similar to the reported spectrum in previous series^[1,13,16,17]. However, there is wide variation in the reported frequencies of different histological subtypes. Fundic gland polyps and hyperplastic polyps are the most prevalent types of gastric polyps in the current literature^[1,2,16]. This was found in our study as well. We found 29% prevalence of hyperplastic polyps and 28% prevalence of fundic polyps. In addition, our data confirmed the positive association between *H. pylori* infection and hyperplastic polyps compared to fundic gland polyps.

There are several subtypes of gastric polyps which can be classified based on their endoscopic appearance or histopathological features. One of the most popular classifications is dividing the gastric polyps into two categories; epithelial and subepithelial. Epithelial

polyps include fundic gland polyps, hyperplastic polyps, adenomatous polyps, polyps associated with familial adenomatous polyposis (FAP) and Peutz-Jeghers syndrome. Subepithelial polyps include gastrointestinal stromal tumors (GISTs), inflammatory fibroid polyps, pancreatic heterotopia, leiomyomas, neuroendocrine tumors and granular cell tumors^[17].

In our study, hyperplastic polyps were the most frequent subtype of polyps. We found a strong association between hyperplastic polyps, chronic gastritis and *H. pylori* infection which confirms what was reported in other studies^[18,19]. A higher prevalence of *H. pylori* infection has been documented in Hispanics living in United States-Mexico border regions compared with non-border areas, which may explain the relatively high prevalence of hyperplastic polyps in our study population^[14,15,20,21]. The risk of dysplasia and neoplastic progression of hyperplastic polyps is controversial with wide discrepancy between the reported rates (1.9% to 19%)^[19,22-24]. However, this type of polyp has been reported to have an increased risk of neoplasia in the surrounding abnormal mucosa and is associated with higher incidence of synchronous gastric cancer^[3,25]. In our series, 11 out of 87 patients who were found to have hyperplastic polyps, had follow-up endoscopy with a mean duration of 30 ± 18 mo. Five (45%) of these 11 patients were found to have residual polyps in follow up endoscopy and none (0%) of them developed dysplasia or cancer. Given this higher risk of developing adenocarcinoma in the surrounding mucosa of hyperplastic polyp, the guidelines recommend obtaining multiple biopsies of the intervening mucosa^[26]. Polyp resection has been recommended for any hyperplastic polyp greater than 0.5 cm in size. Repeat surveillance endoscopy is recommended at 1 year after endoscopic resection^[22,27,28]. Regression of hyperplastic polyps has been reported in many studies after effective treatment of *H. pylori* infection, it is thus essential to treat the patients with active *H. pylori* infection before entertaining any further management^[18,19,29,30] (Figure 1).

FGPs were found to be the second most frequent type of polyp in our study population. The highest prevalence of fundic gland polyps was reported by Carmack *et al*^[11] in a nationwide United States population from 2007-2008 in which FGP constituted 77% of the study cohort. FGP can be found sporadically or in patients with FAP syndrome^[31,32]. Sporadic FGP has been reported in many studies to have a positive association with prolonged use of proton pump inhibitors (PPI)^[33-36]. However, in other series this correlation was not confirmed^[37,38]. Jalving *et al*^[36] reported up to 4-times increased risk of fundic gland polyps with long-term proton pump inhibitor, and Ally *et al*^[33] reported that the duration of PPI therapy greater than 4 years is an independent predictor for FGP development regardless of the used dosage. Due to the retrospective nature of our study, we were unable to obtain accurate data regarding PPI use among the study population. FGPs

have been reported to have a negative association with the presence of *H. pylori* infection^[39]. This was found in our study as well. The risk of dysplasia in sporadic FGPs is rare, while it occurs in 25%-41% of FAP-associated polyps^[31,40]. Biopsy of FGPs is recommended to exclude dysplasia or adenocarcinoma. Polyp resection is recommended for FGPs more than 1 cm in size to eliminate sampling error by missing any neoplastic foci within the polyp^[26,41]. Further workup is recommended to exclude FAP in patients who are less than 40 years of age with numerous FGPs, or if the initial polyp biopsy showed dysplasia^[26].

Raised Intraepithelial Neoplasia is the recent nomenclature for gastric adenomas as they are at increased risk for malignant transformation^[3,42,43]. Three (60%) of the gastric adenomas in our study were associated with underlying atrophic gastritis and intestinal metaplasia which confirms what was reported in other studies^[42,44]. The malignant potential of adenomatous polyps correlates with the polyp size and the age of the patient^[3,24,45-47]. Polyps more than 2 cm in size had been reported to have higher risk of development of adenocarcinoma^[3,45]. The guidelines recommend complete endoscopic removal of gastric adenomas or referral for surgical resection if lesions are not amenable to endoscopic resection or if they contain invasive carcinoma^[26,27]. In addition, careful examination of the rest of the gastric mucosa and obtaining multiple biopsies is recommended to rule out any synchronous neoplastic process. In 2006, the American Society of Gastrointestinal Endoscopy guideline recommended endoscopic surveillance at 1 year for adenomatous polyps. The 2010 British Society of Gastroenterology guidelines recommended to repeat the endoscopic examination at 6 mo for incompletely resected adenomatous polyps or those with high grade dysplasia^[26,27].

In our series, 20 (6.76%) patients were found to have portal hypertensive gastropathy. Half of these patients were found to have hyperplastic polyps. However, it has been reported that hyperplastic polyps in portal hypertensive patients are pathologically distinct from the typical hyperplastic polyps seen in nonportal hypertensive patients with uncertain malignant potential^[48-52]. Management of portal hypertensive polyps is difficult as patients are at increased risk of post-polypectomy bleeding due to associated thrombocytopenia and coagulopathy. Conservative management and follow up endoscopy has been suggested as a safer strategy than multiple polypectomies^[49,52].

There are some limitations to our study. One of the main drawbacks in our study is the lack of information on PPI use for the study cohort. As a result, we were unable to study the correlation between the various types of gastric polyps and PPI use. Second, this study was designed as a retrospective study with its obvious drawbacks. Although this study was performed in a unique practice setting on the United States-Mexico international border and the database used is significantly large, our results may not be applicable

to all settings as our study is single-center study. However, one of the significant strengths of this study is the fact that the majority of the study population is Hispanic (85%) which may give more insight about the characteristics and the histopathologic features of gastric polyps in Hispanics.

In conclusion, the prevalence of gastric polyps in a predominantly Hispanic population is similar to what has been reported in the literature for other populations. Hyperplastic polyps were significantly associated with positive *H. pylori* status and portal hypersensitive gastropathy. Hyperplastic polyps and FGPs were more prevalent in chronic gastritis, while adenomatous polyps were associated with intestinal metaplasia.

COMMENTS

Background

Gastric polyps are usually asymptomatic and incidentally discovered during endoscopic examination. Determination of gastric polyp type is important as the risk for malignant transformation depends on the histopathological type.

Research frontiers

The relationship between *Helicobacter pylori* (*H. pylori*) and the different types of gastric polyps is not well studied.

Innovations and breakthroughs

This is one of a few studies focused on the prevalence and distribution of gastric polyps in Hispanic populations. Hyperplastic and fundic gland polyps accounted for more than half of the resected polyps in this study. Gastric hyperplastic polyps were significantly associated with positive *H. pylori* status and portal hypertensive gastropathy as compared with fundic gland polyps. Hyperplastic polyps and fundic gland polyps were more prevalent in chronic gastritis, while adenomatous polyps were associated with intestinal metaplasia.

Applications

When Hyperplastic polyp is suspected, biopsy of the surrounding mucosa should be done to rule out *H. pylori* infection. In case of an adenomatous polyp, biopsy of the surrounding mucosa should be done to rule out intestinal metaplasia.

Terminology

FGPs: Fundic Gland Polyps; EGDs: Esophagogastroduodenoscopies.

Peer-review

The manuscript is concise, fluent and well-written. Strengths are the number of cases and the ethnicity orientation of the study group. The main drawback is that there is no new knowledge added, apart from ethnicity-targeted results. However, this is still of notice.

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