ORIGINAL ARTICLE

AG-2022-19
doi.org/10.1590/S0004-2803.202202000-49

Pre-operative screening of *Helicobacter pylori* in bariatric patients: is histopathological analysis necessary?

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Received: 24 January 2022
Accepted: 28 March 2022

Abstract – Background – *Helicobacter pylori* infection has been reported to lead to post-operative complications after bariatric surgery (BS), especially marginal ulcers. The optimal method for pre-operative screening is yet to be determined. **Objective –** To analyze the diagnostic accuracy of the endoscopic urease test for the detection of *H. pylori* in individuals undergoing BS and the main endoscopic and histological changes within this population. **Methods –** A cross-sectional study was carried out based on a database from medical records of 232 individuals who underwent BS between 2016 and 2019 at a tertiary university hospital. Clinical, anthropometric, and endoscopic data were analyzed. The gold-standard method considered to calculate diagnostic accuracy variables was histopathological examination through hematoxylin-eosin/Giemsa stains. **Results –** 87.5% of the participants were female; mean age was 38.5±9.5 years and average body mass index was 37.6±3.8 kg/m^2. The commonest endoscopic finding was gastritis (50.9%) with a predominance of the mild erosive form (25%). Upon histological examination, 59.1% of the participants had confirmed *H. pylori* infection. *H. pylori* infection was associated with higher frequencies of endoscopic duodenitis (23.4% vs 12.6%; P=0.04), histological chronic gastritis (100% vs 56.8%; P<0.0001) and histological acute gastritis (58.4% vs 2.1%; P<0.0001). The urease test had a sensitivity of 79.6% and a specificity of 97.9%, leading to an overall accuracy of 87.1%. **Conclusion** – The endoscopic urease test is highly accurate for pre-operative screening of *H. pylori* infection in individuals who undergo BS. *H. pylori* infection was significantly associated with endoscopic (duodenitis) and histopathological (chronic and active gastritis) changes.

Keywords – Obesity; bariatric surgery; *Helicobacter pylori*; biopsy; urease.

INTRODUCTION

The importance of detecting and treating *Helicobacter pylori* infection before bariatric surgery remains controversial. There is extensive evidence showing that *H. pylori* infection in patients undergoing bariatric surgery increased the risk of marginal ulcers and the relapse of previous symptoms such as abdominal pain, reflux, nausea, and vomiting. In a study that enrolled 560 patients, the diagnosis and pre-operative treatment of *H. pylori* reduced the incidence of marginal ulcers from 6.8% to 2.4%, reducing the risk of surgical re-approach caused by perforation, persistent pain, or bleeding secondary to ulcers[1]. According to the 2013 American Society for Metabolic & Bariatric Surgery consensus, pre-operative screening with upper gastrointestinal endoscopy (UGE) for *H. pylori* should be individualized and is more warranted in areas with a higher prevalence of infection[2]. On the other hand, the 2020 consensus of the International Federation for the Surgery of Obesity – European Chapter does not recommend pre-operative screening[3]. Nevertheless, this consensus recommends routine pre-operative UGE related to the need for adjunct treatments and changes in surgical tactics due to endoscopic findings.

The most common endoscopic methods for identifying *H. pylori* are the urease test and histopathological examination. The endoscopic urease test consists of selecting a medium with urea; depending on the presence of bacteria in the collected material, pH changes to alkaline due to the breakdown of urea and ammonia by urease, causing the color of the medium to change. The biopsy for histology should be taken from the antrum and body, and the staining usually used is hematoxylin and eosin, with improved accuracy through special stains such as Giemsa. UGE with biopsy is the most widespread method, although its cost/benefit has not been clearly demonstrated over other methods[4].

This study aims at analyzing the diagnostic accuracy of the endoscopic urease test for the detection of *H. pylori* in individuals undergoing bariatric surgery and describing the main endoscopic changes observed, the prevalence of *H. pylori* infection and identifying the main clinical, endoscopic, and histological changes associated with *H. pylori* infection within this population.

METHODS

Study design

A cross-sectional study was carried out based on a database from medical records of individuals who underwent bariatric surgery between 2016 and 2019 at a tertiary university hospital. Participants were selected through an electronic database of this facility.

Declared conflict of interest of all authors: none
Disclosure of funding: no funding received
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Study population

Individuals who underwent bariatric surgery indicated through the National Institutes of Health consensus, of any gender and aged 18–70 years old were included[5]. Individuals with previous or current history of gastric neoplasms, belonging to vulnerable groups, with recent use of nonsteroidal anti-inflammatory drugs, with previous or current use of alcohol and illicit drugs, who underwent recent *H. pylori* eradication treatment and with incomplete medical records were excluded.

Of 251 individuals who fulfilled the inclusion criteria, 19 were excluded due to incomplete medical records; 232 remained as the study population. A flowchart of the study population is shown in FIGURE 1.

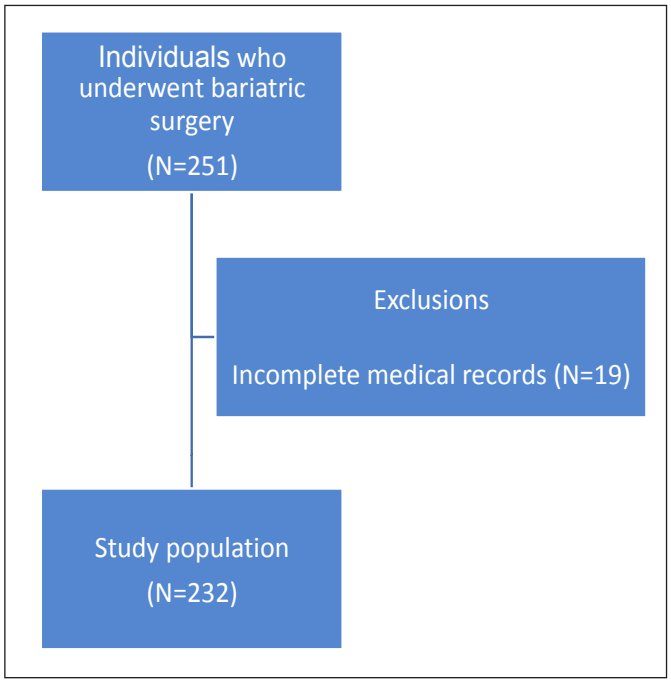

FIGURE 1. Flowchart of the study population.

All individuals in this facility undergo a mandatory weight loss program before bariatric surgery. Surgery is performed when an average 10 to 20% weight loss is achieved.

Study variables

Demographic and Anthropometric data

Data related to the age and gender of the study participants were analyzed, as well as the body mass index at baseline and at the time of surgery.

Clinical variables

The presence of comorbidities in the study population were analyzed. These data were based on information obtained from the medical records of the participants.

Endoscopic data

UGE was performed as part of the pre-operative assessment protocol of individuals undergoing bariatric surgery and data obtained from these examinations were analyzed.

The endoscopic findings considered were: esophagitis, defined as the presence of visually detected inflammatory changes in the distal esophagus (classified as non-erosive or erosive; when erosive, it was classified according to the Los Angeles criteria as A, B, C or D); gastritis, defined by the presence of visually detected inflammatory changes in the stomach (classified as non-erosive or erosive and graded according to intensity as mild, moderate or severe); duodenitis, defined by the presence of visually detected inflammatory changes in the duodenum (classified as non-erosive or erosive and graded according to intensity as mild, moderate or severe); hiatal hernia, defined by the presence of a gastroesophageal transition above the diaphragmatic clamping; peptic ulcers, defined by the presence of lesions ≥3 mm with significant depth in the gastric or duodenal mucosa (classified according to their degree of activity according to Sakita staging classification as active, healing or scar); polyps, defined by the presence of exophytic or sessile lesions projected from the gastric mucosa. The exams were performed by multiple endoscopists from the same UGE team and followed a standardized protocol[6,7].

Histopathological data

The following histopathological variables were considered: esophagitis (defined by the presence of a chronic or acute inflammatory infiltrate in the esophageal tissue); gastritis (defined by the presence of a chronic or acute inflammatory infiltrate in the gastric tissue); duodenitis (defined by the presence of a chronic or acute inflammatory infiltrate in the duodenal tissue); glandular atrophy (defined as the reduction or loss of glands in the gastric mucosa); intestinal metaplasia (defined as the presence in the esophageal or gastric epithelium of goblet cells similar to those seen in the small intestine). These findings were classified according to their severity as mild, moderate, or severe. The analyzes were performed by multiple pathologists from the same pathology team and followed a standardized protocol.

Identification of *H. pylori* infection

Infection by *H. pylori* was investigated using samples endoscopically extracted from the mucosa of gastric antrum and body. Histopathological diagnosis was based on the direct visualization of bacteria under microscopy after staining with hematoxylin-eosin and Giemsa.

The urease test screening was based on placing a fragment of endoscopically extracted gastric mucosa in a tube or gel containing urea and a pH indicator (phenol red); the pH of this solution is 5.9. If urease produced by *H. pylori* is present in the fragment, hydrolysis of the urea occurs, forming ammonia. Ammonia alkalizes the medium, promoting a color change from yellow to pink.

Statistical analysis

The chi-square or Fisher's exact tests were used to compare proportions. To assess the diagnostic methods, diagnostic accuracy tests were used (sensitivity, specificity, positive predictive value, negative predictive value, positive and negative likelihood ratios, overall accuracy); the diagnosis of *H. pylori* infection according to histopathological examination with hematoxylin-eosin and Giemsa stains was considered the gold standard. Normality assessment was performed using the Shapiro-Wilk test. To compare continuous measures, ANOVA was used for variables with normal distribution and Mann-Whitney for non-Gaussian distribution. The significance level adopted was 5% ($P<0.05$). For statistical analysis, the SAS System for Windows (Statistic Analysis System), version 9.2 was used; SAS Institute Inc., 2002-2008, Cary, NC, USA.

RESULTS

Demographic and anthropometric data

Of 232 participants, 203 (87.5%) were female. Mean age was 38.5±9.5 years and the average initial body mass index (BMI) was 43.1±5.4 kg/m^2, while the BMI at the time of surgery was 37.6±3.8 kg/m^2.

Clinical variables

The main comorbidities observed were hypertension (41.8%), type 2 diabetes (16.4%) and dyslipidemia (18.1%).

Endoscopic data

Among the endoscopic findings, 118 (50.9%) patients were diagnosed with gastritis with a higher prevalence of mild erosive form (25%) followed by mild non-erosive (10.7%) and moderate erosive (9 %). Duodenitis was diagnosed in 19.4% of the patients, mostly in its erosive form (19.3%) followed by the non-erosive form (12.5%).

Of the 38 (16.4%) patients with esophagitis, 71.1% had the grade A erosive form, followed by 23.7% with the grade B and 15.2% with the grade C; there were no cases of non-erosive or grade D erosive forms. Only 2.2% individuals had hiatal hernia, and 60% of them were less than 3-cm long. Peptic ulcers were observed in 3% patients, 77% gastric and 23% duodenal, with no identification of activity in both. The highest prevalence of polyps occurred in the stomach (9.1%); there was only 1 (0.4%) case of duodenal polyp. TABLE 1 presents the complete results of the endoscopic findings.

Histopathological data

Chronic gastritis on histopathological examination was present in 82%, while 35% were diagnosed with acute gastritis. Other findings were glandular atrophy (15.5%), fundic gland polyps (9%), intestinal metaplasia (3.4%), and chronic duodenitis (1.7%). Only 13% presented with a normal mucosa.

H. pylori infection

Upon histological examination, 59.1% of the participants had confirmed *H. pylori* infection. Comparing demographic, anthropometric, clinical, endoscopic, and histopathological variables between patients with and without this infection, it was observed that *H. pylori* infection was associated with significantly higher frequencies of endoscopic duodenitis (23.4% vs 12.6%; P=0.04), histological chronic gastritis (100% vs 56.8%; P<0.0001) and histological acute gastritis (58.4% vs 2.1%; P< 0.0001). On the other hand, significantly lower frequencies of endoscopic erosive esophagitis (11.7% vs 23.2%; P=0.02) and gastric polyps (4.4% vs 15.8%; P=0.002) were observed. The complete comparison between the groups with and without *H. pylori* infection is shown in TABLE 2.

The diagnostic accuracy of the urease test compared to the gold standard (histopathology) was evaluated, with a sensitivity of 79.6% and a specificity of 97.9%, leading to an overall accuracy of 87.1%. TABLE 3 show the complete accuracy analysis.

DISCUSSION

In the present study, the average initial BMI of patients corresponded to the observed in other studies; on the other hand, in relation to the BMI at the time of surgery, a significant weight loss before surgery was observed, which corresponded to an average reduction of 14%; this weight loss occurred because of the preoperative mandatory weight loss program adopted at this facility.

TABLE 1. Main endoscopic findings of the study population.

Endoscopic Findings	N (%)	Classification		N (%)
Gastritis	118 (50.9%)	Non-erosive		
		Mild		25 (10.7%)
		Moderate		9 (3.8%)
		Severe		0
		Erosive		
		Mild		60 (25%)
		Moderate		21 (9%)
		Severe		3 (1.2%)
Duodenitis	45 (19.4%)	Non-erosive		
		Mild		7 (3%)
		Moderate		2 (0.8%)
		Severe		0
		Erosive		
		Mild		25 (10.7%)
		Moderate		9 (3.8%)
		Severe		2 (0.8%)
Esophagitis	38 (16.4%)	Non-erosive		0
		Erosive grade A		27 (11.6%)
		Erosive grade B		9 (3.8%)
		Erosive grade C		2 (0.8%)
		Erosive grade D		0
Hiatal Hernia	5 (2.2%)	< 3 cm		3 (1.2%)
		≥ 3 cm		2 (0.8%)
Peptic Ulcer	9 (3.9%)		Sakita classification	
		Gastric	A1	0
			A2	1 (0.4%)
			H1	1 (0.4%)
			H2	2 (0.8%)
			S1	3 (1.2%)
			S2	0
		Duodenal	A1	0
			A2	0
			H1	0
			H2	1 (0.4%)
			S1	1 (0.4%)
			S2	0
Polyps	22 (9.5%)	Gastric		21 (9%)
		Duodenal		1 (0.4%)

N: number of individuals; A1: active with elevated margins; A2: active with discrete margins; H1: healing (<50% covered with regenerative epithelium); H2: healing (almost covered by regenerative epithelium); S1: red scar; S2: white scar.

TABLE 2. Comparison of demographic. anthropometric. clinical. endoscopic. and histopathological characteristics between individuals with or without H. pylori infection.

	No *H. pylori* infection	*H. pylori* infection	Value of *P*
N	95 (40.9%)	137 (59.1%)	NA
Age (years)	37.6±9	39.1±9.9	0.2
Gender	F: 79 (83.2%) M: 16 (16.8%)	F:124 (90.5%) M: 13 (9.5%)	0.1
BMI (kg/m^2)	37.6±4.7	36.8±6	0.3
Comorbidities			
Hypertension	38 (40%)	59 (43.1%)	0.6
Type 2 diabetes	13 (13.7%)	25 (18.2%)	0.3
Dyslipidemias	12 (12.6%)	30 (21.9%)	0.07
Endoscopic findings			
Erosive esophagitis	**22 (23.2%)**	**16 (11.7%)**	**0.02**
Gastritis (overall)	41 (43.2%)	77 (56.2%)	0.05
Non-erosive gastrites	13 (13.7%)	21 (15.3%)	0.7
Erosive gastritis	28 (29.5%)	56 (40.9%)	0.08
Duodenitis (overall)	**12 (12.6%)**	**32 (23.4%)**	**0.04**
Non-erosive duodenitis	1 (1%)	8 (5.8%)	0.07
Erosive Duodenitis	11 (11.6%)	24 (17.5%)	0.2
Gastric Ulcer	3 (3.2%)	4 (2.9%)	0.9
Duodenal Ulcer	1 (1%)	1 (0.7%)	0.8
Atrophic Gastritis	4 (4.2%)	5 (3.6%)	0.8
Hiatal Hernia	2 (2.1%)	3 (2.2%)	0.6
Gastric polyps	**15 (15.8%)**	**6 (4.4%)**	**0.002**
Histopathological findings			
Chronic gastritis	**54 (56.8%)**	**137 (100%)**	**<0.0001**
Active gastritis	**2 (2.1%)**	**80 (58.4%)**	**<0.0001**
Glandular atrophy	13 (13.7%)	23 (16.8%)	0.5
Intestinal metaplasia	3 (3.2%)	5 (3.6%)	0.8
Chronic duodenitis	1 (1%)	3 (2.2%)	0.5

N: number of individuals; BMI: body mass index.
Bold indicates statistical significance.

TABLE 3. Analysis of diagnostic accuracy of urease test.

Variable	Value	95% Confidence interval
Sensitivity	79.6%	71.8%–86%
Specificity	97.9%	92.6%–99.7%
Positive likelihood ratio	37.8	9.6–149.3
Negative likelihood ratio	0.2	0.2–0.3
Positive predictive value	98.2%	93.2%–99.5%
Negative predictive value	76.9%	70. 5%–82.2%
Overall accuracy	87.1%	82.1%–91.1%

With regard to general endoscopic findings, there was a significant involvement of the gastric mucosa, with 50% of patients diagnosed with gastritis in its different forms; 16.4% had changes in the esophagus. The main endoscopic finding was mild erosive gastritis (25%), followed by grade A erosive esophagitis (11%). Only 3.9% had a diagnosis of peptic ulcer, with only one case classified as active. Data from other studies in bariatric populations demonstrated this high prevalence of abnormal endoscopic findings. According to an American review carried out from 2011 to 2017, of 636 patients undergoing pre-operative UGE, 68.7% had esophagitis in different degrees of involvement, with 32.5% having hiatal hernia and 21.9% having esophagitis. Considering the histological findings, gastritis was the most frequent with 68.2% of involvement; esophagitis was confirmed in 84% of patients with endoscopic alterations. In that study, 6 (1%) patients were diagnosed with gastric tumors, four benign (lipoma and leiomyoma) and two malignant (gastrointestinal stromal tumor and adenocarcinoma)[6,7]. In a Brazilian study that enrolled 717 patients from 2007 to 2012, it was observed that 8% of patients had hiatal hernia, but without significant correlation with BMI levels. Also in the same study, 18.7% of patients had esophagitis in different degrees, with a positive relationship between erosive esophagitis and BMI. It is possible that, in the present study, the occurrence of alterations related to gastroesophageal reflux disease has been lower than expected due to pre-operative weight loss, since individuals only underwent endoscopic examinations at a time close to surgery. It is known that weight loss and dietary adjustments are associated with improvement in gastroesophageal reflux disease and are even considered part of the therapeutic guidelines for these patients[8].

The current study identified a high prevalence of histopathologically confirmed *H. pylori* infection. With regards to histopathological abnormalities associated with *H. pylori* infection, glandular atrophy was present in 15% and intestinal metaplasia in 0.03%. There were no suspicious lesions for neoplasms reported, as well as histopathological findings of dysplasia or malignancy. A systematic review enrolling studies performed in 62 countries from 1970 to 2016 showed a 48.5% prevalence of *H. pylori* infection; based on regional prevalence estimates, by 2015 4.4 billion individuals were believed to be infected worldwide[9]. A recent Cochrane review reported a mean prevalence of *H. pylori* infection of 53.7% was reported, and according to another study, the mean prevalence in Brazil was 71.2%[10-14].

In the current study, *H. pylori* was significantly correlated with endoscopic duodenitis, histological chronic gastritis and histological active gastritis. The association between *H. pylori* infection and gastritis and duodenitis is consensual in the literature, largely reinforced by high-level evidence according to the 2015 Kyoto Consensus[15]. On the other hand, the presence of *H. pylori* was a protective factor for endoscopic esophagitis and gastric polyps in the current study. Ashkatorab et al. have previously demonstrated this association between *H. pylori* infection and protection against esophagitis; it is believed that this protection is caused by the effects of *H. pylori* on ghrelin secretion, as well as on gastric acid secretion, which would decrease in the long term. Smith et al., in an exploratory study, had also suggested that *H. pylori* infection could really exert this protective effect. Likewise, there was previous evidence that the prevalence of fundic gland polyps was inversely related to *H. pylori* infection, in contrast to hyperplastic polyps. It is believed that the activity of proteases produced by bacteria act in the degradation of gastric mucus and prevent cystic gland dilatation in these patients[16-19].

Furthermore, the prevalence of *H. pylori*-related abnormalities in the current study was evident; in a context of patients who will undergo bariatric surgery, especially gastric bypass, pre-operative screening followed by eradication should be considered mandatory by our group, in order to avoid post-operative complications, improve dyspeptic symptoms (abdominal pain, reflux and nausea and vomiting) and because of the increased anatomical difficulty for endoscopic evaluation after the procedure, since most of the stomach will be excluded from food transit in gastric bypass procedures.

The quest for lower costs and simpler methods to identify *H. pylori* may lead to benefits in bariatric practice. The overall accuracy of the endoscopic urease test was 87.1%, with sensitivity of 79.6% and specificity of 97.9%. Based on the results of the present study, it is proposed that there is no need for histological analysis of all patients who will undergo bariatric surgery, with the urease test being sufficient for this purpose. In this situation, the performance of biopsy and histopathological evaluation would be reserved for selected cases, in which there are endoscopic alterations that require this analysis, such as suspicious lesions for cancer or specific alterations. Since the accuracy of both methods are comparable and the cost/benefit ratio of the urease test being superior to gastric biopsy, with less costs, less need for medical and hospital resources, especially the pathology team, in addition to being able to demonstrate immediate results.

CONCLUSION

The endoscopic urease test is highly accurate for pre-operative screening of *H. pylori* infection in individuals who will undergo bariatric surgery. Endoscopic abnormalities and *H. pylori* infection were frequent in the study population. *H. pylori* infection was significantly associated with endoscopic (duodenitis) and histopathological (chronic and active gastritis) changes.

Authors' contribution

Valadares EC: collected the data and wrote the first draft of the paper. Gestic MA: provided critical intellectual inserts. Utrini MP: provided critical intellectual inserts. Chaim FDM: provided critical intellectual inserts. Chaim EA: supervised the data collection and provided critical intellectual inserts. Cazzo E: conceived, designed, and performed the analysis and wrote the final draft of the paper.

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Valadares EC, Gestic MA, Utrini MP, Chaim FDM, Chaim EA, Cazzo E. Pesquisa pré-operatória de infecção por *Helicobater pylori* em pacientes bariátricos: a análise histopatológica é necessária? Arq Gastroenterol. 2022;59(2):275-80.

RESUMO – Contexto – A infecção por *Helicobacter pylori* tem sido descrita como causa de complicações pós-operatórias após cirurgia bariátrica (CB), especialmente úlceras marginais. O método ideal para a triagem pré-operatória ainda não foi determinado. **Objetivo –** Analisar a acurácia diagnóstica do teste endoscópico de urease para detecção de *H. pylori* em indivíduos submetidos à CB e as principais alterações endoscópicas e histológicas observadas nessa população. **Métodos –** Foi realizado um estudo transversal a partir de um banco de dados de prontuários de 232 indivíduos submetidos à CB entre 2016 e 2019 em um hospital universitário terciário. Dados clínicos, antropométricos e endoscópicos foram analisados. Foi considerado como método padrão-ouro para calcular as variáveis de acurácia diagnóstica o exame histopatológico por colorações de hematoxilina-eosina e Giemsa. **Resultados –** 87,5% dos participantes eram do sexo feminino; a média de idade foi de 38,5±9,5 anos e o índice de massa corporal médio foi de 37,6±3,8 kg/m^2. O achado endoscópico mais comum foi gastrite (50,9%) com predomínio da forma erosiva leve (25%). Ao exame histológico, 59,1% dos participantes apresentaram infecção confirmada por *H. pylori*. A infecção por *H. pylori* foi associada a maiores frequências de duodenite endoscópica (23,4% vs 12,6%; *P*=0,04), gastrite crônica histológica (100% vs 56,8%; *P*<0,0001) e gastrite aguda histológica (58,4% vs 2,1%; *P*<0,0001). O teste de urease teve sensibilidade de 79,6% e especificidade de 97,9%, levando à acurácia global de 87,1%. **Conclusão –** O teste endoscópico de urease tem alta acurácia para triagem pré-operatória da infecção por *H. pylori* em candidatos à CB. A infecção por *H. pylori* foi significativamente associada a alterações endoscópicas (duodenite) e histopatológicas (gastrite crônica e ativa).

Palavras-chave – Obesidade; cirurgia bariátrica; *Helicobacter pylor*i; biópsia; urease.

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