

## Esophagitis and esophageal motor abnormalities in patients with chronic spinal cord injuries

J G Stinneford MD, A Keshavarzian MD, B A Nemchausky MD, M I Doria MD, M Durkin MD

*Departments of Medicine and Pharmacology, Loyola University Medical Center, Maywood, Illinois; Medical, Spinal Cord Injury and Pathology Services, Hines Veterans Hospital, Hines, Illinois, USA.*

To investigate the frequency and severity of esophagitis and esophageal dysmotility in patients with chronic spinal cord injury (SCI), 46 males with chronic SCI completed a questionnaire regarding gastrointestinal symptomatology. Eleven of these patients subsequently underwent upper gastrointestinal (GI) endoscopy with esophageal biopsies and 10 of the 11 also had esophageal motility studies. A significantly higher percentage of SCI patients experienced heartburn (SCI 61%; controls (C) 40%), esophageal chest pain (SCI 33%; C 6.4%), and intermittent dysphagia (SCI 30%; C 8.5%). Forty-five percent of SCI patients had endoscopic evidence of mild esophagitis, and 91% of them had histologic evidence of esophagitis. SCI patients had low amplitude, slowly propagating abnormal (double-peaked) peristaltic esophageal contractions. We conclude that SCI patients experience significantly more esophageal symptoms than controls. They have a higher incidence of esophagitis and esophageal motor abnormalities. The clinical relevance of these abnormalities remains to be evaluated.

*Keywords:* spinal cord injury; reflux esophagitis; esophageal motor abnormalities; gastrointestinal symptomatology.

### Introduction

Spinal cord injuries (SCI) represent a significant worldwide health problem, most often affecting young, otherwise healthy individuals. Historically, a spinal cord injury meant a rapid, progressive downhill course with death ensuing secondary to pulmonary, urinary or infectious complications.<sup>1–3</sup> Fortunately, advances in the management of the acute injury have led to a marked decline in overall mortality since World War II.<sup>3,4</sup> However, inherent in this longevity is the subsequent development of related comorbid disease which can significantly alter the quality of life.

One area of concern in this population is chronic gastrointestinal dysfunction and as-

sociated complications. Recent studies have demonstrated an increased incidence of abnormalities in the upper gastrointestinal tract, particularly gastric and duodenal ulceration, erosions and bleeding.<sup>5–9</sup> These disorders may produce greater morbidity because severe cord injury can alter somatic perception thereby delaying diagnosis and therapy.<sup>6,7,9</sup> One might also expect patients with SCI to be at a greater risk for esophageal disease. A number of factors may predispose these individuals to gastroesophageal reflux with its associated sequelae. First, they spend a greater proportion of time in the supine or semi-upright position. Second, esophageal motor abnormalities have been described in other patient groups suffering from chronic myelopathies<sup>10</sup> and if present may diminish acid clearance. Third, the majority of these patients will demonstrate increased intraabdominal pressure more frequently because of chronic constipation, frequent valsalva maneuvers

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Correspondence: Ali Keshavarzian MD, Associate Professor of Medicine, Section of Gastroenterology, Loyola University Medical Center, 2160 South First Avenue, Maywood, IL 60153, USA.

and use of abdominal musculature for transfers. Esophageal function and disease in spinal cord injured patients has not previously been systemically evaluated.

For these reasons we designed a study with the following aims: (1) to determine the frequency of gastrointestinal and esophageal complaints following long-standing spinal cord injury; (2) to determine whether patients with chronic stable spinal cord injuries have a higher incidence of esophagitis and, if so, to delineate the extent and severity of the inflammation; and (3) to assess esophageal motor function in this population.

## Methods and patients

### *Patient population*

Subjects consisted of male patients admitted to the SCI service of Hines Veterans Hospital. All of the SCI were greater than one year in duration and all were judged to be neurologically stable. None of the subjects had been admitted to the unit for problems related to the gastrointestinal tract. SCI levels ranged from C5 to T10. Subjects were excluded if they suffered from illnesses known to alter gastroesophageal motor function such as diabetes mellitus or scleroderma or if they required chronic medication known to affect GI motility (including benzodiazapines and anticholinergics). A questionnaire was given to 46 consecutive SCI patients and following its completion all were asked to undergo esophagogastroduodenoscopy (EGD) and esophageal motility testing. Eleven of the 46 agreed to participate in endoscopy and 10 of the 11 agreed to undergo motility studies.

### *Questionnaire*

A detailed questionnaire was administered to 46 consecutive SCI males in order to quantify the nature and intensity of any long-standing GI symptomatology. Data were compared with 47 male controls of similar ages admitted to the Veterans Hospital with medical problems unrelated to the GI tract. GI complaints evaluated included frequency of defecation as well as presence and severity of heartburn, nausea, vomiting, dysphagia, chest pain of esophageal origin

(defined as food related and/or relieved with antacids), fullness after meals and abdominal pain. A severity index was calculated using the product of the frequency of a given symptom per week and its severity (assessed by a visual analog of 0–10). Each patient was asked whether he had a given symptom (regardless of its severity) during the last year. If the answer was positive, then he was asked to determine the frequency of the episodes of the symptom (regardless of the duration of severity) per week. Then he was asked to indicate the severity of the symptom (regardless of its frequency) by marking on a 10 cm graduated line. The questionnaire was administered to each and every patient by one of the authors (JGS).

### *Assessment of esophagitis*

Upper GI endoscopy (EGD) was performed on 11 male volunteers with chronic SCI as defined above (age range 25–60); mean 50.5 yrs). These subjects were similar to the remaining 32 patients with regard to age as well as frequency and severity of GI symptoms (Table I). The results were compared with 18 asymptomatic males admitted to the Veterans Administration alcohol detoxification unit (age range 31–60; mean 44 yrs). These alcoholic controls happened to have no esophageal symptoms regularly (monthly) at the time of the EGD. Their last alcoholic drink was at least 3 days (range 3–14 days) prior to the EGD. Prior to undergoing EGD all subjects were asked to fast overnight. Intravenous sedation was achieved with midazolam (Roche Laboratories, Nutley, NJ). The oropharynx was anesthetized with tetracaine applied topically. An Olympus GIFXQ10 endoscope (Olympus, Lake Success, NY) was utilized and three forceps pinch biopsies were obtained at each of two sites 2 cm and 5 cm above the gastroesophageal junction. Endoscopic appearance was graded according to previously published criteria.<sup>11</sup> The grading scale was as follows: grade 0, no mucosal abnormalities; grade 1, no macroscopic erosions but erythema, hyperemia, or mucosal friability; grade 2, superficial erosions involving < 10% of the mucosal surface of the last 5 cm of esophageal squamous mucosa;

**Table 1** Frequency and severity of esophageal symptoms in patients with spinal cord injury (SCI) who agreed or refused to have endoscopy

	Heartburn		Esophageal chest pain		Acid reflux frequency	Dysphagia frequency
	Frequency	SI	Frequency	SI		
SCI patients undergoing endoscopy (n = 11)	6/11 (55%)	10 (range 0.5-49)	3/11 (27%)	5 (range 0.67-10)	5/11 (45%)	4/11 (36%)
SCI patients refusing endoscopy (n = 35)	22/35 (63%)	7 (range 0.6-36)	12/35 (34%)	6 (range 0.8-17.5)	14/35 (40%)	10/35 (29%)

There was no significant difference in frequency or severity of esophageal symptoms between patients with spinal cord injury (SCI) who underwent upper GI endoscopy and those who refused endoscopy. SI = severity index was calculated as product of frequency (number of symptoms episode per week)  $\times$  severity of symptoms. Frequency = number of patients experiencing the symptom.

grade 3, superficial erosions or ulceration involving 10-50% of the mucosal surface of the last 5 cm of esophageal squamous mucosa; grade 4, deep peptic ulceration anywhere in the esophagus or confluent erosion of > 50% of the mucosal surface of the last 5 cm of esophageal squamous mucosa. All three biopsy specimens from each of two sites were oriented on filter paper and histologic evaluation was performed by an investigator blinded to the endoscopic findings. The presence of histologic esophagitis was assessed according to previously reported criteria.<sup>12-14</sup> Esophagitis was considered to be present if both the basal cell layer and papillae were hypertrophied to greater than 50% of the specimen thickness. The presence of neutrophils in the lamina propria was considered to be supportive evidence of esophagitis.

#### *Assessment of esophageal motility*

Ten of the 11 SCI subjects evaluated for reflux esophagitis also underwent esophageal manometry. One subject refused further investigation. These data were compared with a control group which consisted of 13 healthy male asymptomatic volunteers (age range 24-39; mean 31 yrs). Esophageal manometry was performed utilizing an eight-lumen esophageal catheter with a 6 cm Dent sleeve and high-pressure, low-compliance infusion system (Arndorfer Medical Specialists Inc, Greendale, WI). Intraluminal pressures were transmitted by water-filled catheters to external transducers (Sensormedics Transducers and Dynograph, Anaheim, CA). The recording catheters were arranged to measure pressure through side orifices, spaced at 3 cm intervals. The infusion rate was 0.5 ml/min at each orifice. Sensitivity of the system was 400 mmHg/s. Lower esophageal sphincter pressure (LESP) was measured by a Dent sleeve. Intra-gastric pressure was continuously measured by a catheter distal to the sleeve and LESP was measured against intra-gastric pressure which was considered to have a value of zero. Peristaltic amplitude, duration and velocity in response to wet swallows (5 ml intraoral water bolus) at 30-second intervals were assessed at 3 cm, 6 cm and 9 cm above the LES.

*Statistical analysis*

The statistical significance of the results was assessed by the Mann-Whitney *U* test when GI symptomatology/symptom indexes were compared between SCI patients and controls, and chi-square when the frequency of symptoms were compared. The frequency of esophagitis was compared utilizing the chi-square test and differences in motility results were analyzed with Student's *t* test. A probability value of  $<0.05$  was considered significant.

**Results***Frequency and severity of gastrointestinal symptoms*

Patients with chronic SCI reported a significantly higher number of GI complaints when compared to controls, especially with regard to esophageal symptomatology (Table II). A significantly higher percentage

of SCI patients reported heartburn, dysphagia, esophageal chest pain and abdominal pain. In addition, their symptoms were significantly more frequent and more severe than controls (Table III). Eleven of 28 symptomatic SCI patients (39%) had weekly heartburn and 20 patients (71%) had monthly heartburn. In contrast, only 3 (16%) and 9 (47%) of symptomatic controls had weekly and monthly heartburn respectively. Similarly, 7 (47%) and 9 of 15 (60%) symptomatic SCI patients had weekly and monthly esophageal chest pain respectively; while one of 3 symptomatic controls had weekly chest pain. Frequent abdominal pain was also significantly more common in symptomatic SCI patients: 17 of 24 (71%) had weekly pain and 20 (83%) had monthly pain. Monthly abdominal pain was reported by 3 controls.

Nausea, vomiting and postprandial fullness were not significantly different between the two groups. None of the 46 SCI patients

**Table II** Frequency of GI symptoms in patients with spinal cord injury (SCI)

	Heartburn frequency	Esophageal chest pain frequency	Abdominal pain frequency	Dysphagia frequency
SCI patients ( <i>n</i> = 46)	28/46 <sup>a</sup> (61%)	15/46 <sup>a</sup> (33%)	24/46 <sup>a</sup> (52%)	14/46 <sup>a</sup> (30%)
Controls ( <i>n</i> = 47)	19/47 (40%)	3/47 (6.4%)	4/47 (8.5%)	4/47 (8.5%)

Significantly higher numbers of patients with spinal cord injuries (SCI) reported episodes of heartburn, esophageal chest pain and dysphagia than control groups. Frequency = number of patients experiencing the symptom. <sup>a</sup>*p* < 0.05 SCI patients versus controls.

**Table III** Severity of GI symptoms in patients with spinal cord injury (SCI)

	Heartburn		Esophageal chest pain		Abdominal pain	
	Frequency of episodes	SI	Frequency of episodes	SI	Frequency of episodes	SI
SCI patients ( <i>n</i> = 46)	1.3 <sup>a</sup>	7.2 <sup>a</sup>	1.3 <sup>a</sup>	4.6 <sup>a</sup>	3.1 <sup>a</sup>	16.2 <sup>a</sup>
Controls ( <i>n</i> = 47)	0.4	5.8	0.4	2.4	0.7	4.8

Patients with SCI reported significantly more severe and more frequent episodes of heartburn, chest pain, and abdominal pain. SI = severity index = frequency/week × visual analog scale. Frequency of episodes = number of symptom episodes per week. <sup>a</sup>*p* < 0.05 SCI patients versus control subjects.

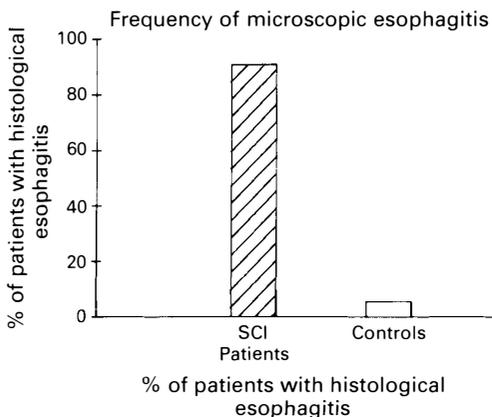
had spontaneous bowel movements and each required a specific program of bowel care to minimize constipation.

*Assessment of esophagitis*

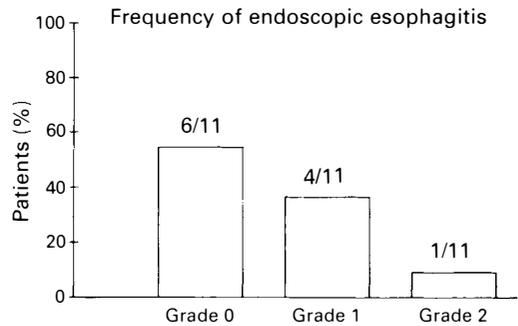
In the SCI group 91% (10 of 11) demonstrated histologic evidence of significant esophagitis compared to 6% (1 of 18) of asymptomatic controls (Fig 1). Every SCI patient judged to have reflux esophagitis met all three histologic criteria in at least one biopsy specimen. The endoscopic findings did not correlate well with the histologic evaluation. One subject received an endoscopic score of 2 and 4 additional subjects received a score of 1. The remaining 6 had normal appearing esophageal mucosa (Fig 2). No esophageal stricture was noted in any of the patients studied. None of the 18 control subjects demonstrated endoscopic evidence of esophagitis.

*Assessment of esophageal motility*

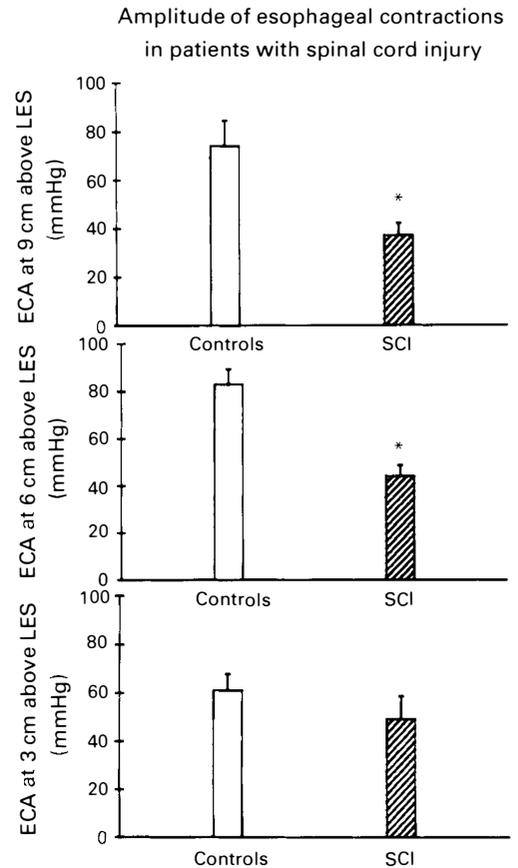
The esophageal contraction amplitude (ECA) in SCI patients was significantly lower than in controls when measured at 9 cm and 6 cm above the LES (Fig 3). ECA at 3 cm above the LES was also lower than in controls but this difference was not statistically significant. The esophageal contraction velocity (ECV) in SCI patients was significantly slower than in controls only in



**Figure 1** Patients with chronic spinal cord injuries (SCI) demonstrated a significantly higher frequency of histologic esophagitis.



**Figure 2** Endoscopic grading of esophageal mucosa in spinal cord injured patients correlated poorly with histologic findings.



**Figure 3** The esophageal contraction amplitude (ECA) was significantly lower in spinal cord injured patients at 9 cm and 6 cm above the LES but not at 3 cm.

the proximal esophagus (Fig 4). The esophageal contraction duration was similar in both groups. Sixty percent of the SCI patients demonstrated a higher frequency of double-peaked contractions (defined as greater than 20% of total contractions) compared to 5% of controls. Of the increased double-peaked contractions in the SCI group, 50% occurred in the proximal esophagus, 17% in the distal esophagus and 33% throughout the esophagus. Thirty percent of the SCI group also demonstrated repetitive contractions compared to none of the controls. No significant differences were noted in LESP or percent of LES relaxation in response to swallowing between either group (Table IV).

### Discussion

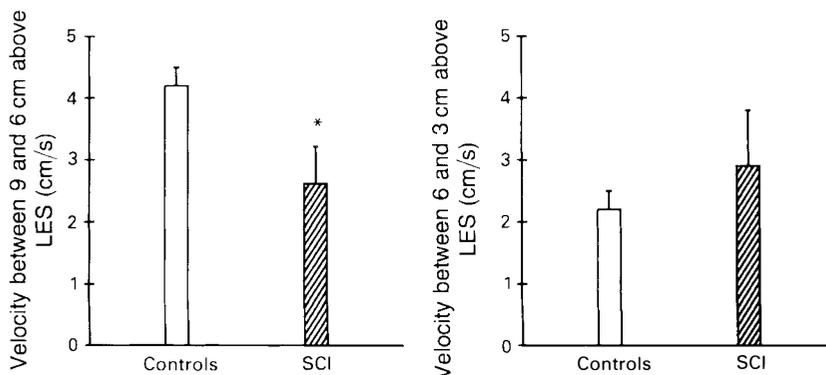
As the initial resuscitation and management of acute spinal cord injuries continue to improve, more SCI patients may develop chronic, often debilitating sequelae to their injuries. The chronicity of these problems merely adds to the overall frustration and depression most individuals experience after SCI, a fact which may be reflected in the rising suicide rate amongst younger SCI patients.<sup>1</sup> In addition, while overall mortality has declined, life expectancy remains lower than normal, with such cause-specific deaths as pulmonary and cardiovascular disease being more frequent than age-matched controls.<sup>1,2</sup> For these reasons, it is desirable to better delineate the nature and

extent of comorbid disease in SCI patients so that appropriate long-term treatment strategies can be developed.

In this study we addressed one such health concern—namely, gastroesophageal reflux disease (GERD). We also attempted to better define GI complaints, especially those related to the esophagus, in the context of a chronic SCI. Esophageal motor function was assessed because of the close relationship between abnormal esophageal motility and GERD in patients without SCI.

Gerd is a common entity within the general population and one would expect this to hold true for SCI patients as well. Indeed our study demonstrated the presence of mild esophagitis in a high percentage of SCI patients. The underlying cause of this problem is not clear. However, many aspects of the cord injury would seem to place these patients at a higher risk for reflux. A number of recent studies have demonstrated that GERD likely represents a multifactorial process with inflammation occurring secondary to imbalances between esophageal acid exposure and mucosal protection.<sup>15–17</sup> These imbalances become particularly important when considering the SCI population.

Dent *et al* noted that induction of transient lower esophageal sphincter relaxation (TLESR) in normal subjects with artificially increased intraabdominal pressure led to significant reflux episodes approximately 80% of the time.<sup>16</sup> Similarly, Holloway and colleagues elicited a marked increase in



**Figure 4** The esophageal contraction velocity was significantly slower proximally in spinal cord injured patients. No difference was noted in the distal esophagus.

**Table IV** Demographic characteristics and esophageal findings in patients with spinal cord injury (SCI)

Patient	Age	Level of injury	Esophageal symptoms <sup>a</sup>	Histologic esophagitis	Macroscopic grading	LESP (mmHg)	Esophageal contraction amplitude <sup>b</sup> (mmHg)	Esophageal contraction velocity (9 to 6 cm/s)
1	48	T4-5	H	Yes	1	14	6 cm = 75 9 cm = 41	4.7
2	57	T10	None	Yes	1	23	6 cm = 43 9 cm = 43	1
3	54	C5-6	None	Yes	0	18	6 cm = 37 9 cm = 25	2.9
4	25	C5-6	H, D, E	Yes	1	20	6 cm = 59 9 cm = 64	1.4
5	32	T5-6	H, A	Yes	2	16	6 cm = 56 9 cm = 26	4.6
6	56	T5-6	H, D, E, A	Yes	0	12	6 cm = 32 9 cm = 30	1
7	58	T9	H, D, E	Yes	0	13	6 cm = 35 9 cm = 48	3.2
8	60	T2-3	D, A	Yes	0	13	6 cm = 30 9 cm = 10	5
9	57	C5-6	H, A	Yes	0	14	6 cm = 31 9 cm = 27	3
10	58	C5-6	A	Yes	0	17	6 cm = 48 9 cm = 58	1.5
11	66	T5-6	None	No	0	ND	ND	ND

<sup>a</sup>H = heartburn, D = dysphagia, E = esophageal chest pain, A = acid reflux. <sup>b</sup>Amplitude and velocity of esophageal contraction measured at 6 cm and 9 cm above LES; normal: 9 cm =  $74 \pm 11$  mmHg, 6 cm =  $85 \pm 6$  mmHg, 9 to 6 cm =  $4.2 \pm 0.3$  cm/s. LESP = lower esophageal sphincter pressure. ND = not done.

TLESR in both normals and patients with documented reflux when intragastric pressure was increased with balloon distension.<sup>18</sup> These findings would appear to be significant in the setting of a chronic SCI because, as stated in the introduction, these patients demonstrate frequent episodes of increased intraabdominal pressure. This elevation in intraabdominal pressure could, therefore, predispose these patients to more frequent TLESR with the subsequent reflux of gastric contents into the esophageal lumen. This concept is supported by the observations of Gore and coworkers who noted an increased frequency of gastroesophageal reflux in SCI patients undergoing barium studies.<sup>5</sup> However, studies with 24-hour esophageal pH measurement is needed to determine whether gastroesophageal reflux is more frequent or more severe in these patients. We initially planned to perform 24-hour pH studies in our patients. Unfortunately, none of our patients agreed to undergo such a test.

Another important pathophysiologic component of reflux esophagitis is the length of exposure of esophageal mucosa to gastric contents. Studies have shown that esophageal acid clearance is dependent on normal primary peristaltic function (volume clearance) and acid neutralization with salivary bicarbonate.<sup>19</sup> Kahrilas *et al* demonstrated a positive correlation between peristaltic dysfunction and ineffective volume clearance from the esophageal lumen.<sup>20</sup> Therefore, esophageal dysmotility may increase the risk of reflux esophagitis by diminishing acid clearance. Esophageal motor abnormalities have been described in patients with chronic myelopathies<sup>10</sup> but have not been previously studied in the SCI population.

In the present study, both the amplitude and the velocity of esophageal contractions were significantly lower in SCI patients than in controls. The SCI group also demon-

strated a higher frequency of abnormal contractions which may contribute to overall peristaltic dysfunction. Similar esophageal motor disturbances have been described in patients with GERD.<sup>17</sup> These abnormalities may increase the acid exposure time, but direct measurement of acid clearance in the SCI population is necessary for confirmation.

It is also possible that these motor abnormalities are a consequence of reflux disease rather than causative. Our study cannot exclude this possibility since our control subjects had no esophagitis. Further studies are needed to compare esophageal motility SCI patients with esophagitis with SCI patients without esophagitis.

The LES and percent LES relaxation were normal in our SCI group. This is not unexpected given the fact that vagal innervation remains intact in the majority of cord injuries.

Interestingly, chronic SCI patients did not experience more nausea, vomiting or postprandial fullness implying that clinically significant gastric dysmotility may not be present in the majority of SCI patients. This is supported by a recent study demonstrating normal gastric emptying in chronic SCI patients.<sup>21</sup>

Finally, the endoscopic mucosal grading correlated poorly with the presence or absence of histologic esophagitis in our study. This is not surprising and is consistent with other studies comparing endoscopic appearance to histologic evaluation, especially when the inflammatory changes are mild.<sup>22</sup>

It remains to be seen whether early recognition of gastroesophageal reflux combined with prompt intervention in the disease process will decrease aspiration pneumonia and other complications of GERD as well as significantly improve the lives of patients with chronic spinal cord injuries.

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