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SURGICAL ENDOSCOPY
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Significant weight loss after laparoscopic Nissen fundoplication

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Abstract
Background: Laparoscopic Nissen fundoplication (LNF) has evolved as a gold standard in antireflux surgery. However, the association between body weight and gastroesophageal reflux disease (GERD) is still unclear, and no data are available concerning the effect of fundoplication on body weight. We present the first report elucidating the impact of LNF on body weight in GERD patients with special emphasis on patients' quality of life.
Methods: From July 2000 to March 2003, LNF was carried out in 213 patients (85 women and 128 men) after thorough preoperative examination including clinical interview with standardized assessment of symptoms and quality of life (QoL), endosocopy, barium swallow, 24-h pH-metry, and manometry. Follow-up investigations were performed 3 and 12 months after LNF obtainable from 209 patients (98.1%) and 154 patients (72.3%), respectively.
Results: The mean body mass index (BMI) decreased significantly after LNF (27.6 ± 5.6 kg/m^2 before LNF vs 26.0 ± 3.8 kg/m^2 after LNF, $p < 0.001$). Twelve months after LNF, neither a tendency toward a renewed increase nor a further decrease in BMI was observable. The average body weight loss was 3.9 kg. BMI reduction was higher in women than in men ($p < 0.002$), and obese patients lost more weight than lean patients ($p < 0.001$). There was no association between BMI reduction and dysphagia. Plasma cholesterol and triglyceride levels did not change after LNF. The mean general score of the Gastrointestinal Quality of Life Index markedly improved (90.1 ± 21.3 before LNF vs 118.0 ± 16.2 after LNF, $p < 0.01$), as did the GERD-Health Related Quality of Life Index (21.9 ± 6.4 before LNF vs 3.5 ± 2.7 after LNF, $p < 0.001$). However, there was no association between changes in BMI and QoL.
Conclusion: LNF leads to significant and persistent body weight loss.

Key words: Gastroesophageal reflux — Laparoscopic fundoplication — Nissen — Body mass index — Weight reduction — Quality of life

Gastroesophageal reflux disease (GERD) is the most common upper gastrointestinal disorder in the Western world affecting up to 44% of the adult population. Increasing prevalence of at least occasional reflux symptoms ranges from 12 to 54%, whereas the prevalence of refluxesophagitis varies from 30 to 79% [17]. The sequelae, such as esophageal stricture formation (5%), ulceration (4%), Barrett's esophagus (3.5%), along with the increasing incidence of adenocarcinoma in patients with Barrett's esophagus (up to 2.1%) [17], remain challenging topics in gastroenterology and gastroesophageal surgery.

With the introduction of minimally invasive surgery for the treatment of GERD in the early 1990s, referrals for surgery have dramatically increased. Laparoscopic Nissen fundoplication (LNF) is the most common minimally invasive antireflux procedure [4] because it has been shown to be 96% successful in relieving the primary symptoms for which the surgery is performed [16]. Even at long-term follow-up, more than 90% of the patients were still free of the initial symptoms [9], and patients' satisfaction rate was more than 96% after 6.4 years [1]. Further advantages of laparoscopical procedures, such as minimal morbidity, early recovery, and superior esthetic outcome, are widely accepted. To date, LNF is still the gold standard in antireflux surgery, despite endoluminal therapies gaining increasing attention [15].

Numerous studies have tried to elucidate the association between body weight and GERD. However, the influence of body mass index (BMI) on GERD symp-

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toms remains uncertain as different studies have obtained controversial results [10]. Patients frequently report that they lost weight after LNF, although they do not suffer from dysphagia. No data are available describing the effect of fundoplication on body weight.

The aim of this study was to prospectively evaluate body weight changes after LNF in a consecutive series of patients with emphasis on the patients' quality of life (QoL).

Materials and methods

Patient selection

Between July 2000 and March 2003, 224 patients with typical symptoms of GERD underwent LNF, which represents 22.3% of all patients assessed for GERD symptoms. Of the 224 patients, eight requiring refundoplication because of scarring (three patients) and slipping (five patients) were excluded. Two patients who had to be operated on for cancer and one patient with a severe postoperative complication were excluded from the study as well. Thus, a total of 213 patients (85 women at a mean age of 53.0 ± 11.4 years and 128 men at a mean age of 45.7 ± 11.5 years) with primary intervention were included in this study. None of them suffered from eating disorders or consuming diseases, which may have affected patients body weight. The study was performed according to the guidelines of "Good Scientific Practice" by the Medical University of Vienna.

All patients had a thorough preoperative evaluation including clinical interview with standardized assessment of their symptoms. Body weight and height were evaluated and BMI (weight in kilograms divided by the square of height in meters) was calculated [8]. Barium esophagogram, upper gastrointestinal endoscopy with biopsy and histologic assessment, 24-h esophageal pH monitoring, and esophageal manometry completed the preopative evaluation.

Indication for surgery in our patients was determined as follows: long history of GERD-related symptoms, persistent or recurrent GERD-related symptoms despite adequate treatment with proton pump inhibitors (PPIs) (20–80 mg of PPIs daily), persistent or recurrent complications of GERD, reduced QoL, and pathological lower esophageal pressure (< 8 mmHg). Patients with poor esophageal motility underwent fundoplication as described by Toupet and were not included in this study. Demographic data are shown in Table 1.

A "floppy" LNF was performed according to the standard technique [16]. Oral intake was started on the day of operation. Patients were not put on a special diet but were advised to chew thoroughly. They were usually discharged between 2 and 7 days (median, 4) after the operation.

Quality of life

Disease-related QoL was evaluated using the German version of the Gastrointestinal Quality of Life Index (GIQLI) [5] according to the recommendations of the European Study Group for Antireflux Surgery [7] and the GERD-Health Related Quality of Life Index (GERD-HRQLI) [21]. Follow-up investigations were performed 3 and 12 months after surgery, following the same protocol as preoperatively.

Statistical analysis

Statistical analysis was performed using the SAS software system V8.2 (SAS Institute, Cary, NC, USA). Results are expressed as mean ± standard deviation or as median (interquartile range). To examine the change of BMI and the QoL scores over time, analysis of variance (ANOVA) with the fixed factor time (before LNF and 3 and 12 months after LNF), sex, the random factor patient, and the interaction between time and sex was performed. Subsequently, post hoc comparisons between time points were performed according to Tukey's studentized range test. To test whether the change in BMI depends on the baseline value, the correlation coefficient of the 3 months minus baseline differences and the means of these two values were tested against zero. Pearson's correlation coefficient (r) was used to assess the relationship between "parameters of interest." Likewise, the association between change in QoL (expressed as 3 months minus baseline difference) and the change of the BMI (3 months minus baseline difference) was evaluated. Comparisons of clinical symptoms and endoscopic, pH-metric, and manometric data at the different time points were assessed by the ANOVA model defined previously and by McNemar's test. Due to the explorative nature of these analyses no adjustment for multiple comparisons was performed. A p value < 0.05 was considered to indicate statistical significance.

Table 1. Demographic data of GERD patients[a]

No. of patients	213
Gender (male/female)	128 (60.1%)/85 (39.9%)
Mean age (yr)	49 ± 12
Mean period of GERD symptoms (yr)	8.5 ± 4.6
No. of symptomatic patients despite PPI intake	180 (84.5%)
No. of patients taking PPI	212 (99.5%)
Mean period of PPI (20–80 mg/daily) intake (mo)	19.5 ± 9.1
No. of patients taking prokinetic agents	42 (19.7%)
Mean period of prokinetic agents intake (mo)	4.6 ± 3.8
Height (cm)	171 ± 8
Body weight (kg)	79.7 ± 12.7
Body mass index (kg/m^2)	27.6 ± 5.6
Cholesterol (mg/dl)	216 ± 43
Triglycerides (mg/dl)	128 ± 74

GERD, gastroesophageal reflux disease; PPI, proton pump inhibitors
[a] Data are given as mean ± standard deviation or absolute number and percentage

Results

Surgical and clinical outcome

Demographic data are shown in Table 1. Proton pump inhibitors were taken by 99.5% of the patients and 84.5% suffered from persistent or recurrent GERD-related symptoms despite adequate medical treatment. Patients' major complaints were epigastric pain (98.2%), regurgitation (65.7%), and respiratory problems (36.5%).

Three months postoperatively, all but four patients had been reevaluated and almost all of them underwent endoscopy and pH- and manometry (Table 2). Typical GERD symptoms significantly decreased ($p < 0.05$ for all symptoms in comparison to preoperative). The relief of patients' symptoms was paralleled by the improvement of the endoscopic and pH- and manometric findings (Table 2). Esophagitis was less frequently found 3 months after LNF ($p < 0.05$ for all grades). Hiatal hernia was seen in 80.1% of patients before surgery, but it was hardly detectable 3 months after LNF (4%, $p < 0.01$). In these patients a slight slipping of the fundoplicate was observed, but most patients were free of GERD symptoms. Therefore, no further intervention was required. Manometry revealed an impressive improvement in resting lower esophageal sphincter (LES)

Table 2. Barium swallow, endoscopic, pH-metric, and manometric results before and 3 and 12 months after LNF[a]

Clinical evaluation	Before LNF, n = 213 (100%)	3 mo after LNF, n = 209 (98.1%)	12 mo after LNF, n = 154 (72.3%)
Endoscopy (Savary–Miller)	213 (100%)	203 (97.1%)	115 (74.7%)
No esophagitis	10 (4.7%)	153 (75.4%)	86 (74.8%)
Esophagitis I	23 (10.8%)	2 (1.0%)	1 (0.9%)
Esophagitis II	36 (16.9%)	0	1 (0.9%)
Esophagitis III	16 (7.5%)	0	3 (2.6%)
Esophagitis IV	56 (26.3%)	21 (10.3%)	6 (5.2%)
Barretts' esophagus	72 (33.8%)	27 (13.3%)	18 (15.6%)
Barium swallow	201 (94.4%)	199 (95.2%)	107 (69.5%)
Hiatal hernia	161 (80.1%)	8 (4.0%)	7 (6.5%)
Manometry	212 (99.5%)	201 (96.2%)	109 (70.8%)
Intraabdominal length (cm)	1.0 ± 0.8	2.6 ± 0.8	2.4 ± 0.7
Resting LES pressure (mmHg)	6.6 ± 5.2	19.2 ± 6.3	18.6 ± 6.0
Impaired motility	20 (9.4%)	13 (6.5%)	9 (8.3%)
24-h pH-metry	210 (98.6%)	189 (90.4%)	108 (70.1%)
DeMeester score	25.8 (16.0–41.2)	3.7 (1.4–7.3)	3.4 (1.4–7.0)
Reflux time (pH <4 in %)	6.7 (3.7–10.4)	0.8 (0.2–1.6)	0.6 (0.2–1.6)

LNF, laparoscopic Nissen fundoplication; LES, lower esophageal sphincter
[a] Data are given as means ± standard, median (interquartile range) or absolute number and percentage

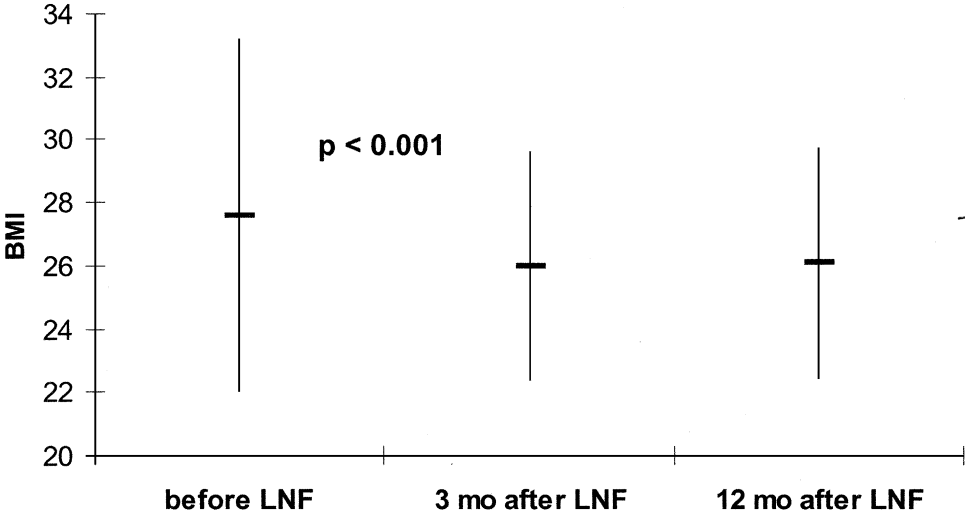

Fig. 1. Body mass index (BMI) before and 3 and 12 months after laparoscopic Nissen fundoplication (LNF). Data are given as mean ± standard deviation.

pressure ($p < 0.01$) as given in Table 2. Concurrently, the more physiologic anatomy of the esophagogastric zone was measurable in the increase of the intraabdominal length of the esophagus after surgery ($p < 0.05$). Twenty-four-hour pH-metry showed a shift from the highly pathologic DeMeester score preoperatively toward physiologic levels along with the reduction of the reflux time ($p < 0.01$ for both parameters) (Table 2).

Twelve months after surgery, clinical evaluation was obtainable from 72.3% of the patients. However, only 74.7 and 70.8% of the patients were willing to undergo endoscopy and pH- and manometry, respectively. Those patients who could not be evaluated by endoscopy and pH- and manometry were all free of any GERD symptoms and highly satisfied with the operation's outcome.

Body weight and lipid changes

The mean BMI of our patients was 27.6 ± 5.6 kg/m^2 before LNF. Three months after LNF, BMI has significantly decreased (26.0 ± 3.6 kg/m^2, $p < 0.001$), and there was no tendency toward a renewed increase in BMI 1 year postoperatively ($p = 0.94$) (Fig. 1). The average reduction of body weight was 3.9 kg. Nineteen patients (9.1%) did not reduce weight and 19 patients (9.1%) showed a slight increase in body weight (average, 2.4 kg).

Women had a slightly higher BMI (28.1 ± 4.9 kg/m^2) than men (26.9 ± 3.3 kg/m^2) preoperatively. Body weight loss was significantly higher in females (28.1 ± 4.9 kg/m^2 before LNF vs 26.5 ± 4.3 kg/m^2 3 months after LNF) than in males (26.9 ± 3.3 kg/m^2 before LNF vs 25.7 ± 3.0 kg/m^2 3 months after LNF) ($p < 0.002$).

The change in BMI depends on the baseline BMI, meaning that overweight and obese patients lost significantly more weight than lean subjects. The correlation coefficient (r) between the change in BMI and the mean of the initial BMI is −0.32 ($p < 0.001$). This relation is shown in Fig. 2. There was no association between loss of body weight and rate of dysphagia (observed in eight patients) 3 months after LNF.

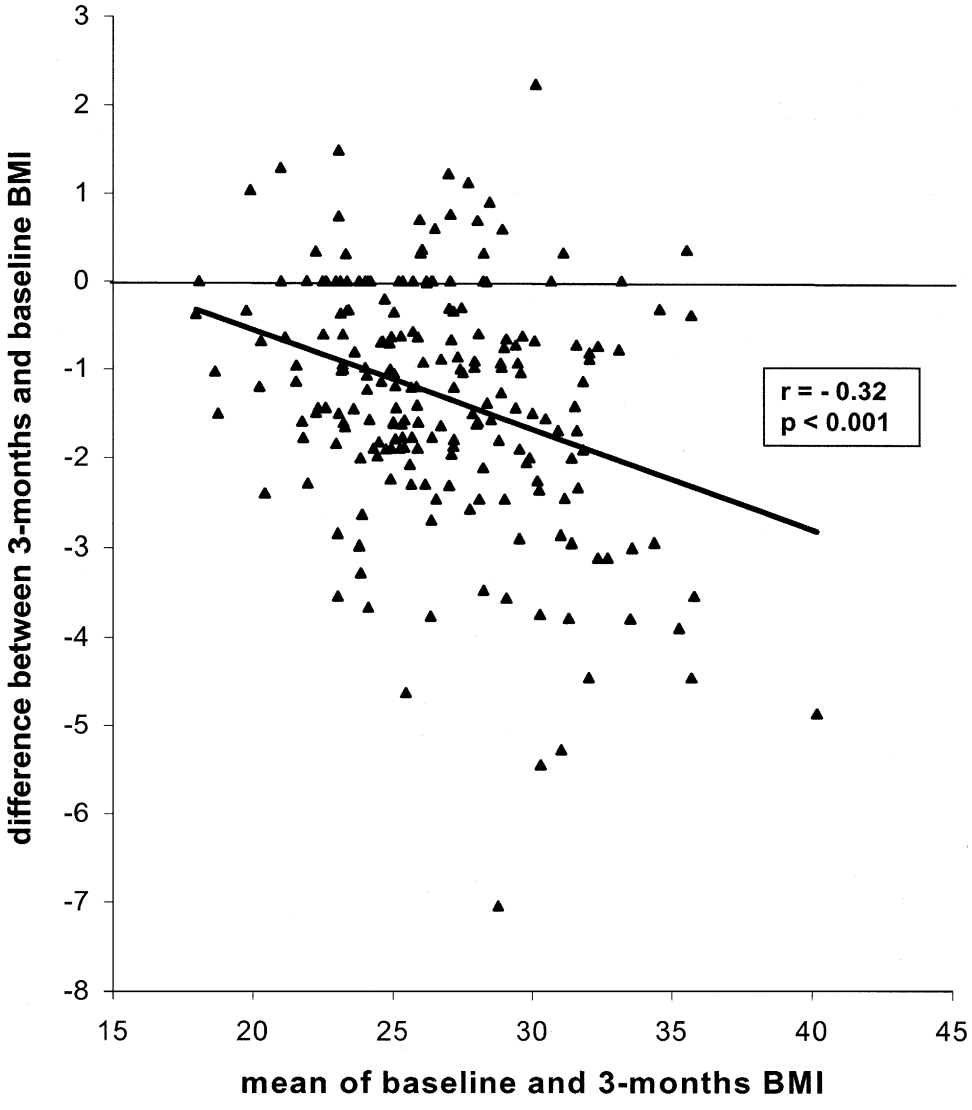

Fig. 2. Correlation between change in body mass index (BMI) 3 months after laparoscopic Nissen fundoplication and the mean of the initial BMI.

Plasma cholesterol levels and triglycerides (Table 1) did not change significantly during the follow-up period, nor was there any difference regarding these parameters between patients who lost weight and those who did not.

Quality of life

The QoL data were available only from fewer patients because QoL was not assessed before May 2002. Before surgery, the mean GIQLI score (90.1 ± 21.3) was significantly impaired compared with the mean score of healthy controls (122.6 ± 8.5). Three months after surgery, the mean general score increased significantly (118.0 ± 16.2, $p < 0.01$) and did not change 12 months postoperatively. Likewise, the GERD-HRQLI improved significantly (21.9 ± 6.4 before LNF vs 3.5 ± 2.7 3 months after LNF, $p < 0.001$). One year after LNF the score was almost the same (3.3 ± 2.8).

There was no association between changes in QoL and change in BMI ($p = 0.67$ for GIQLI and $p = 0.37$ for GERD-HRQLI, respectively). Additionally, no statistically significant difference in QoL was detectable when patients with weight reduction were compared to those who remained stable or gained weight.

Discussion

A significant reduction in body weight after LNF was observed in this study (Fig. 1), possibly due to postoperative dysphagia. Kamolz et al. [11] reported that >50% suffered from dysphagia 1 week after surgery. However, 3 months postoperatively, the number of patients without swallowing disorders increased to >90%, and only 2% exhibited severe dysphagia [11]. Therefore, it seems unlikely that the reduction in body weight 3 months after LNF is attributable to dysphagia. In our series, dysphagia was reported by eight patients (3.9%) 3 months after LNF and there was no statistically detectable association between body weight loss and dysphagia. A slight slipping of the fundoplicate was observed in two of the eight patients reporting dyspha-

gia. However, there was no reflux detectable in pH-metry and manometry 3 months postoperatively. Twelve months after surgery, they were both free of symptoms. A further patient suffered from diffuse esophageal spasms and his dysphagia improved after medical treatment with a calcium channel blocker. The five other patients reporting dysphagia confessed dietary mistakes and were referred for a further educational interview by our dietitian.

Patients are taught to severely modify their eating habits after LNF. They are advised to take smaller bites and to chew thoroughly. Modifications of eating behavior have been described as a central determinant of whether people will lose weight and maintain the loss [2]. Comprehensive behavioral approaches have been shown to result in mean weight losses of up to 4 kg [23]. Likewise, in our series the mean weight reduction was 3.9 kg, which is a further indication that modification of eating behavior may be the major reason for weight reduction after LNF. Although weight loss after LNF is relatively small, it may be enough to improve many obesity-related conditions [23]. Moreover, a dose-dependent association between increasing BMI and reflux symptoms has been described [14]. Consequently, a reduction in body weight may, at least in part, contribute to the good results after LNF, especially regarding long-term results [1, 9]. The fact that BMI reduction after LNF was dependent on baseline BMI can be explained by an even more pronounced effect of modification of eating behaviors in overweight and obese persons.

A slight increase in body weight after LNF is expected because most patients suffer from epigastric pain preoperatively, and many of them cannot eat sweets or drink alcohol, both high-caloric substances, because they would further aggravate their epigastric complaints. It has been shown that alcohol stimulates acid secretion and gastrin release and inhibits LES, thus enhancing gastroesophageal reflux [10]. Our follow-up interviews indicated that many patients were able to drink alcohol after LNF because they no longer suffered from epigastric pain.

Early satiety has been described as a side effect of LNF [6, 9]. However, the reported incidence of early satiety varies considerably between 16 and 70.1% [6, 9]. A prolonged period of chewing may contribute to this perception. Nevertheless, the exact mechanism remains unclear, although postprandial fullness has been associated with delayed gastric emptying of solids and also with early satiety and weight loss with postcibal impaired accommodation of the gastric fundus [12, 20]. Lindeboom et al. [12] showed that maximal postprandial fundus relaxation was significantly reduced in patients after LNF, and that there was a positive correlation between the postoperative duration and the degree of postprandial fundus relaxation. However, no significant differences were detectable concerning postprandial fullness among patients after LNF, unoperated GERD patients, and healthy controls [12].

Altered gastric emptying may be a further explanation for body weight loss after LNF. It has been shown that LNF leads to a transitory increase in gastric emptying, which is related to a simultaneous decrease in gastric volume and compliance [3]. However, long-term weight loss is unlikely to be explained by these findings because in the model investigated gastric emptying returned to preoperative levels 30 days after LNF [3]. Nissen fundoplication has been reported to have a vagolytic effect on the lower esophageal sphincter [18]. Consequently, enhanced emptying is likely when the LES pressure is reduced. Likewise, impaired receptive relaxation of the gastric cardia after LNF has been described [22].

Women lost significantly more weight than men. This finding might be explained by the fact that a strong association between high BMI levels and GERD was found only in women [14]. Female hormones, increased levels of estrone in fatty tissue, and altered nitric oxide levels that influence LES relaxations are the causes of these gender-specific results [14]. Women had a higher BMI preoperatively than men in our study. Because BMI reduction was also dependent on the baseline BMI (Fig. 2), this may be another explanation for the higher weight loss in female patients.

Serum cholesterol and triglyceride levels did not change throughout the follow-up period. Many lifestyle variables, such as fitness, BMI, percentage of body fat, nicotin and alcohol consumption, as well as hormones (oral contraceptives and hormon replacement therapy), influence the lipid profile [19]. Therefore, detailed analyses including HDL and LDL cholesterol are necessary to determine the effect of body weight loss after LNF on lipid profiles in select groups of patients.

QoL has been markedly improved after LNF, which is in accordance with the literature [13, 21]. However, there was no correlation between body weight loss and changes in QoL. This further supports the finding that body weight loss after LNF is not associated with postfundoplication symptoms such as dysphagia. Otherwise, QoL for patients with weight loss should have been worse than for those with stable or increasing body weight.

In conclusion, this is the first study attempting to elucidate the influence of LNF on body weight. LNF leads to a significant but small reduction of approximately 4 kg 3 months after surgery, and there is no tendency toward a renewed increase within 12 months after LNF. The BMI reduction depends on the baseline BMI and gender, and there is no association between the rate of dysphagia and body weight reduction, also supported by the similar improvement in QoL in patients with weight loss and those without. These findings should be taken into account when patients are informed of LNF preoperatively. Further investigations are necessary to define predictive factors concerning body weight loss and the importance of body weight loss on long-term functional results after LNF.

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