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Evaluation of a Clinical Outcome of Resistant Gastroesophageal Reflux Disease after Treatment with Full Thickness Endoscopic Device

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ABSTRACT

Background: The widespread chronic illness known as gastroesophageal reflux disease (GERD) significantly lowers quality of life (QOL). Additionally, reflux esophagitis and occasionally serious side effects including ulceration, strictures, Barrett's mucosa, and esophageal cancer can be brought on by gastroesophageal reflux disease (GERD).

Objective: To determine the clinical effectiveness of endosural suturing using a gastroscope in patients with refractory GERD.

Patients and methods: This is prospective research that was conducted at Ain Shams University Hospitals' Gastroenterology Outpatient Clinic and Endoscopic Centre. The research was carried out between September 2019 and December 2020 on 25 adult patients with Hiatus hernia or recalcitrant GERD.

Results: After the procedure, 2 (8%) had heart burn, 1 (4%) had regurgitation, 0 (0%) had asthma, 0 (0%) had chronic cough, 0 (0%) had laryngitis, and 0 (0%) had hoarseness. Regarding the severity of symptoms, there was a highly statistically significant difference between the pre- and post-treatment periods. In our investigation, we determined that the mean Hb was 12.89 (± 0.80 SD), the mean RDW was 13.40 (± 0.95 SD), the mean number of platelets (*1000) was 239.76 (± 59.92 SD), and the mean RBCs was 5.19 (± 0.51 SD) based on CBC data. The Gastrointestinal QOL Index showed a very statistically significant difference between the pre- and post-procedure states. Based on our own research, we discovered that the difference in Hill's grade before and after treatment was extremely statistically significant.

Conclusion: According to our study, endoscopic suturing of the gastroesophageal junction significantly improves QOL following the treatment, significantly lessens the intensity of symptoms following the procedure, and significantly improves reflux management for up to six months.

Keywords: GERD, QOL, Full Thickness Endoscopic Device.

INTRODUCTION

One of the most common stomach problems is GERD, which is characterised by the reflux of stomach and duodenal contents into the esophagus, resulting in uncomfortable symptoms and consequences that lower QOL [(1)].

Clinical symptoms can include common ones like heartburn and regurgitation [(2)], as well as unusual ones including asthma, persistent cough, laryngitis, hoarseness, and otitis media when stomach contents pass across the upper esophageal sphincter [(3)]. In addition to impairing the patient's QOL, GERD increases the chance of developing Barret's esophagus and esophageal cancer [(4)].

A complicated pathophysiology including altered reflux exposure, visceral sensitivity, and epithelial resistance underlies GERD. Acid reflux produces symptoms and damages the esophagus [(5)].

The diagnosis of GERD is a challenging process that involves combining upper endoscopy, esophageal pH monitoring, and clinical symptoms [(6)].

The management of GERD includes life style modification such as weight loss, changes in diet and sleeping posture [(7)].

Long-term Proton Pump Inhibitors (PPIs) therapy is one aspect of pharmacological treatment; nevertheless, it is linked with adverse effects, including osteoporosis, small intestine bacterial overgrowth, and renal failure [(8)].

Antireflux surgery (open or laparoscopic fundoplication) has been suggested for management of patients not responding to PPIs, however large percentage of patients restart PPI on long term and require reintervention [(9)].

Other adverse effect may occur with antireflux surgery such as gas bloating, dysphagia. When treating refractory GERD, endoscopic plication is a less invasive alternative to laparoscopic fundoplication that has been shown to be an effective and practical method [(10)].

The goal of this study was to determine the clinical effectiveness of endosural suturing using a gastroscope in patients with refractory GERD.

PATIENTS AND METHODS

This is prospective research that was conducted at Ain Shams University Hospitals' Gastroenterology Outpatient Clinic and Endoscopic Centre. The research was carried out between September 2019 and December 2020 on 25 adult patients with Hiatus hernia or recalcitrant GERD.

Inclusion criteria:

1. Adults (18-75) years old patients from both sexes.
2. Patients with typical reflux symptoms despite treatment with PPI for more than 6 months.
3. Resistant GERD.
4. Hiatus hernia of size less than 2 cm.
5. Patients not fit for prolonged use of PPs.
6. Patients not fit for a surgery.

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Exclusion criteria:

1. Pregnancy.
2. Younger than 18 and older than 75 years old.
3. Patients with large hiatus hernia.
4. Patients with heart failure, renal failure, respiratory failure.
5. Patients with decompensated chronic liver disease.

Sample size: 25 adult patients having resistant GERD.

Methods:

1. Clinical assessment:

a) History: Age, sex, and residence.

Symptoms related to gastroesophageal reflux (heart burn, regurgitation, asthma, chronic cough, laryngitis and hoarseness).

b) Clinical examination.

2. Laboratory assessment: (routine and general evaluation tests)

- Complete blood picture (TLC, RBCs, hemoglobin, RDW, platelets).
- Biochemical liver profile (serum bilirubin, serum aminotransaminases ALT, AST), alkaline phosphatase, serum albumin, prothrombin time).

3. Radiological assessment:

1. Pelvi-abdominal ultrasonography (US).
2. Endoscopic assessment: Gastroscopy before and after procedures assessed by Hill's grade.

Hill's grade:

It has been demonstrated that the Hill's classification is repeatable and offers helpful data for assessing individuals with suspected GERD who are having an endoscopy [(11)]:

Hill's Grade I: a noticeable tissue fold adjacent to the endoscope along the smaller curve. Hill's Grade II: the endoscope is surrounded by moments of quick shutting and opening, and the fold is less noticeable. Hill's Grade III: the tissue is not strongly gripping the endoscope, and the fold is not very noticeable. Hill's Grade IV: there is no fold and the esophageal lumen is open, frequently making it possible to see the squamous epithelium below. There is usually a hiatal hernia [(11)].

QOL evaluation:

The German Gastrointestinal Quality of Life Index (GIQLI) was used to assess QOL [(12)]. The European Study Group for Antireflux Surgery has suggested using this verified German version of the questionnaire [(13)]. With a minimum of 0 and a maximum of 144 points, the GIQLI is broken down into 5 categories and 36 items: gastrointestinal symptoms (0–76 points), physical functions (0–28 points), emotional state (0–20 points), social functions (0–16 points), and a single item for stress of medical treatment (0–4 points). A higher QOL is indicated by higher scores. Data about the regular or sporadic usage of PPIs or other antacid medications was acquired.

Symptom evaluation:

A written questionnaire (Figure 1) was used to conduct a standardised assessment of symptoms, rating the intensity and severity of 14 symptoms on a 4-point scale (SCL). There has been prior usage of this questionnaire in relation to GERD [(14)]. The following are the grades for the symptoms: (a) duration: none (0), once per week (1), several times per week (2), daily (3), and constantly (4); (b) intensity: none (0), mild (1), moderate (2), severe (3), and extremely severe (4); and (c) fullness, diarrhoea, flatulence, constipation, belching, bloatedness, and distortion of taste.

The frequency of each symptom is multiplied by its degree to determine the final score, which ranges from 0 to 16 for each symptom, with a maximum score of 224 points and a minimum score of 0 points. In addition, four distinct scores were collected to evaluate symptoms that are unique to bowel dysfunction (diarrhoea, constipation, flatulence), gas-bloat (fullness, bloatedness), reflux (heartburn, regurgitation, chest pain), and atypical reflux symptoms (cough, hoarseness, asthma, distortion of taste). Belching and dysphagia symptoms are assessed independently.

Number _____ T 00 D 00

Abdominal or Epigastric symptoms

*Did you experience during the **last 4 weeks**:*		none	mild	moderate	quite a lot	severe	very severe	unbearable
1. Abdominal pain	in common	○	○	○	○	○	○	○
	postprandial	○	○	○	○	○	○	○
	fasting	○	○	○	○	○	○	○
	doesn't decline after defecation	○	○	○	○	○	○	○
2. Epigastric pain	in common	○	○	○	○	○	○	○
	during daytime	○	○	○	○	○	○	○
	at night / asleep	○	○	○	○	○	○	○
3. Heartburn		○	○	○	○	○	○	○
4. Regurgitation		○	○	○	○	○	○	○
5. Abdominal rumbling		○	○	○	○	○	○	○
6. Bloating		○	○	○	○	○	○	○
7. Empty feeling		○	○	○	○	○	○	○
8. Nausea		○	○	○	○	○	○	○
9. Vomiting		○	○	○	○	○	○	○
10. Loss of appetite		○	○	○	○	○	○	○
11. Postprandial fullness		○	○	○	○	○	○	○
12. Belching		○	○	○	○	○	○	○
13. Flatulence		○	○	○	○	○	○	○
14. Haematemesis		○	○	○	○	○	○	○
15. Dysphagia	liquid food	○	○	○	○	○	○	○
	solid food	○	○	○	○	○	○	○
16. Stools	melaena	○	○	○	○	○	○	○
	bloody	○	○	○	○	○	○	○
	mucous	○	○	○	○	○	○	○
	frequent hard	○	○	○	○	○	○	○
	diarrhea	○	○	○	○	○	○	○
	alternately solid or loose	○	○	○	○	○	○	○
	constipation	○	○	○	○	○	○	○
	frequently with pain	○	○	○	○	○	○	○
	urging stools	○	○	○	○	○	○	○
	incomplete	○	○	○	○	○	○	○
	steatorrhoea	○	○	○	○	○	○	○

18. Describe your abdominal or epigastric pain during the last 4 weeks by marking the line below with a cross. No text.

no complaints _____ unbearable symptoms

0000000000000000000 3330049989

Figure (1): A copy of the evaluated GI symptoms questionnaire [(14)].

Ethical approval:

Medical Ethics Committee of Ain Shams Faculty of Medicine gave its approval to this study. All participants gave written consent after receiving all information. The Helsinki Declaration was followed throughout the study's conduct.

Statistical analysis

SPSS version 20 was used to analyse the data. In the form of mean±SD, range, median and interquartile range, quantitative variables were stated. The terms number and percent were used to characterise qualitative variables. Utilising the Student t test, parametric quantitative variables were compared between two groups. Fisher's exact test was used to compare qualitative variables. The test for marginal homogeneity was used to examine the significance of differences in Hill's grades between pre- and post-treatment data. P value < 0.05 was considered significant.

RESULTS

The most common age was ≥40 years old, the mean of age was 38.12, 60% were males, and 72% were rurales (Table 1).

Table (1): Distribution of the cases under study based on demographic data (n=25)

Demographic data	No.	%
Age (years)		
10 – <20	2	8.0
20 – <30	5	20.0
30 – <40	6	24.0
≥40	12	48.0
Min. – Max.	18.0 – 58.0	
Mean ± SD.	38.12 ± 13.57	
Median (IQR)	37.0 (25.0 – 52.0)	
Sex		
Male	15	60.0
Female	10	40.0
Residence		
Urban	7	28.0
Rural	18	72.0

Laryngitis and hoarseness were the most common extraintestinal manifestations before treatment. After procedure, the patients were cured from all these manifestations (Table 2).

Table (2): The extraintestinal manifestation of GERD before and after procedure (n=25)

Symptoms		Before ttt	After ttt	P-value
Asthma	No	10 (40.0%)	25 (100.0%)	< 0.001
	Yes	15 (60.0%)	0 (0.0%)	
Chronic cough	No	14 (56.0%)	25 (100.0%)	< 0.001
	Yes	11 (44.0%)	0 (0.0%)	
Laryngitis	No	16 (64.0%)	25 (100.0%)	0.001
	Yes	9 (36.0%)	0 (0.0%)	
Hoarseness	No	16 (64.0%)	25 (100.0%)	0.001
	Yes	9 (36.0%)	0 (0.0%)	

There was highly statistically significant difference according to Hill's grade between before procedure and after procedure in the studied patients (Table 3).

Table (3): Hill's grade in the patient before and after procedure (n=25)

Hill's grade	Before ttt		After ttt		^{MH}p
	No.	%	No.	%	
Grade I	0	0.0	21	84.0	**<0.001***
Grade II	0	0.0	4	16.0	
Grade III	10	40.0	0	0.0	
Grade IV	15	60.0	0	0.0	

MH: Marginal Homogeneity Test.

p: p value for comparing between before treatment and after treatment.

*: Statistically significant at $p \leq 0.05$

There was highly statistically significant difference according to using PPI and antacids between before treatment and after treatment (Table 4).

Table (4): The frequency of using PPI antacids in the patients before and after treatment (n=25)

Using PPI and antacids	Before	After 1 month	After 3 months	After 6 months	P-value
	No. (%)	No. (%)	No. (%)	No. (%)	
No	0 (0.0%)	24 (96.0%)	24 (96.0%)	23 (92.0%)	< 0.001
Yes	25 (100.0%)	1 (4.0%)	1 (4.0%)	2 (8.0%)	

There was highly statistically significant difference according to GIQLI between before procedure and after procedure (Table 5).

Table (5): GIQLI in the patients before and after procedure (n=25)

GIQLI	Before treatment	After treatment	p
Min. – Max.	62.0 – 122.0	104.0 – 133.0	<0.001
Mean ± SD.	94.4 ± 18.42	120.32 ± 8.16	
Median (IQR)	98.0 (78.0 – 109.0)	123.0 14.0 – 126.0)	

t: Paired t-test, p: p value for comparing between before treatment and after treatment. *: Statistically significant at p ≤ 0.05, GIQLI: Gastrointestinal Quality of Life index.

Table (6) shows that according to CBC, the mean of Hb 12.89 (± 0.80 SD), the mean of RDW 13.40 (±0.95 SD), the mean of platelets (*1000) 239.76 (±59.92 SD), mean of RBCs 5.19 (± 0.51 SD).

Table (6): CBC among studied patient (n=25)

CBC	Mean ± SD.
Hb (g/dL)	12.89 ± 0.80
RDW	13.40 ± 0.95
Platelets (*1000)	239.76 ± 59.92
RBCs (mcL)	5.19 ± 0.51

Table (7) shows the liver functions of the studied patients.

Table (7): Descriptive analysis of the studied cases according to liver function (n=25)

Liver function	Mean ± SD.
Serum bilirubin (mg/dl)	0.68 ± 0.16
ALT (IU/L)	27.60 ± 4.71
AST (IU/L)	28.40 ± 7.05
Alkaline phosphatase (IU/L)	103.68 ± 25.61
Serum albumin (g/dL)	4.15 ± 0.54
Prothrombin time	12.60 ± 0.74
Anti HCV Ab	0.0 ± 0.0

DISCUSSION

A frequent chronic illness that significantly lowers QOL is GERD. Additionally, reflux esophagitis and occasionally serious side effects such ulceration, strictures, Barrett's mucosa, and esophageal cancer can be brought on by GERD [(15)].

According to surveys, as many as 15-20% of individuals report having heartburn once a week. Consequently, the expense of medications recommended to treat GERD places a significant financial strain on society. PPIs have drawbacks and restrictions even though they are quite successful in treating esophagitis and reducing common reflux symptoms. They typically cause rebound acid hypersecretion after medication withdrawal and fail to reestablish the natural antireflux barrier at the gastroesophageal junction, both of which increase the high recurrence rate seen following PPI treatment termination [(16)].

Fundoplication is a very effective way to manage GERD and can restore the LOS's competency. Many transendoscopic approaches have been developed recently with the goal of directly correcting poor LES function. The first was the transesophageal endoscopic plication procedure, which was developed by BARD after being first reported by Dr. Paul Swain [(17)].

In this study we found that the mean of age of the studied patients was 38.12 (± 13.57 SD), 15 (60%) were males, 10 (40%) were females, 7 (28%) were urbans and 18 (72%) were rurales.

Whereas, **Tam *et al.*** [(18)] found that the median age was 46 years (range 24–64 years), 46% were males, 54% were females and **Mahmood *et al.*** [(19)] found that median age was 39 years (range 22–62 years) and Male:Female ratio was 15:12.

In this study, we found significant improvement of all symptoms as heart burn severity, frequency, regurgitation, belching, vomiting and nausea. This matches with **Filipi *et al.*** [(20)] who found significant improvements that were noted in regurgitation, heartburn score, frequency, and intensity of heartburn. Patients who were having regurgitation before to the operation saw an improvement in it. Following therapy, none of the patients reported transient dysphagia.

As regard the extraintestinal symptoms of GERD, our study pre-treatment results showed 15 (60%) had asthma, 11 (44%) had chronic cough, 9 (36%) had laryngitis, 9 (36%) had hoarseness, which improved with application of GERDx and reached 0% of all extraintestinal symptoms of GERD.

According to **Barnes *et al.*** [(21)], the incidence of bothersome atypical symptoms decreased significantly after TIF due to morbid obesity. Specifically, coughing (77% vs. 25%, P <.001) and globus sensation decreased from 77% to 12%, hoarseness decreased from 53% to 5%, throat clearing from 82% to 15%, excess throat mucus or postnasal drip decreased from 75% to 15%, and coughing decreased from 70% to 15%.

In this study, we found that 10 patients (40%) had Hill's grade III and 15 patients (60%) had Hill's grade IV before procedure while after procedure, 21 patients (84%) had Hill's grade I and 4 patients (16%) had Hill's grade II and this matches with **Barnes *et al.*** [(21)] who assessed the clinical results of 124 consecutive patients with GERD who underwent TIF. Hill's grade I tight valves were found in 89% of the cases, hiatal hernias were reduced in 33/34 (97%) of the patients, and reflux esophagitis was healed in 25/30 (83%) of the patients after endoscopy.

In our study, according to need to PPI and antacids before and after procedure, we found that all patients (n=25, 100%) used PPI and antacids before procedure. After procedure 24 patients (96%) did not need them in one month and three months follow up, 23 patients (92%) did not need to use PPI and antacids in 6 months. This matches with **DiBaise *et al.*** [22] who found that 13 instances had improved, 3 had remained unchanged, and 1 had gotten worse. Nine out of 14 patients did not require antacids after treatment, compared to just one patient at baseline who did not require antacids as rescue therapy (p 0.001). Antacid intake also considerably decreased after treatment.

Whereas, **Del Piano *et al.*** [23] found that all patients were using PPI/H2B once daily prior to the operation; one month later, five had quit taking it, and two had cut back to fewer than four doses per month. **Tam *et al.*** [18] discovered that all patients were receiving regular acid-suppressant medication prior to endoscopic suturing, and no post-procedure complications transpired. Seven out of fifteen patients (47%) were asymptomatic and not taking any medication, 6 months after endoscopic suturing. Eight patients were kept on acid-suppressive medication at a lower dosage than what was necessary for pretreatment.

Whereas, **Barnes *et al.*** [21] found significantly fewer patients complained about troublesome heartburn (92% versus 19%, P <0.001), regurgitation (85% versus 12%, P <0.001), abdominal distension (76% versus 22%, P <0.001), and dysphagia (68% versus 15%, P <0.001).

In an investigation to assess red cell distribution width and mean platelet volume as possible novel biomarkers in kids with GERD by **Sevencan *et al.*** [24], they found that mean of RDW was 12.70 ± 4.93, mean of Hb was 13.64 ± 0.83 and mean of MPV was 7.67 ± 1.44.

In our study, we discovered a highly statistically significant difference in QOL between before and after treatment, which matches the findings of **Mahmood *et al.*** [19], who discovered a significant improvement in all five QOL parameters at 12-month post-procedure compared to baseline.

This also matches with, **Filipi *et al.*** [20] who discovered that, across all scales, a greater score was found, which denotes a better QOL. The SF-36 QOL questionnaire was given out at baseline and six months following the treatment. **Tam *et al.*** [18] reported that after six months, there was a substantial improvement in both the GERD-HRQoL and the SF-36v2 scale in terms of both symptom intensity and QOL. This improvement was particularly evident in the two subscales, Social Functioning and Bodily Pain. These gains persisted for a full year.

Whereas, **DiBaise *et al.*** [22] found that they did not find any additional improvement in QOL, as measured by the SF-36 survey, six months following treating.

CONCLUSION

According to our study, endoscopic suturing of the gastroesophageal junction significantly improves QOL following the treatment, significantly lessens the intensity of symptoms following the procedure, and significantly improves reflux management for up to six months.

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