# Fundoplication Alone and Class II Obesity or Higher Are Associated with The Need to Restart Proton-Pump Inhibitors After Anti-Reflux Surgery in Patients with Hiatal Hernia

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## BACKGROUND

- Anti-reflux surgeries, including hiatal hernia repair (HHR), or fundoplication (F), improve acid reflux and decrease the need for proton-pump inhibitors (PPIs). Following surgery, most patients can discontinue PPIs. It remains unclear which factors are associated with the restarting of PPIs after their initial discontinuation.

## OBJECTIVE

- We aimed to determine features associated with the discontinuation and subsequent restarting of PPIs in patients with a hiatal hernia (HH) who undergo anti-reflux surgery.

## METHODS

- Retrospective study across four academic centers in Mayo Clinic between January 2015 and December 2021.
- Inclusion criteria: 1) cross-sectional imaging showing hiatal hernia, 2) undergone index anti-reflux surgery (HHR alone, F alone, or HHR+F) at one of our four sites 3) age 18 or older. Exclusion criteria: if any of the above not met
- Wilcoxon Rank Sum and Fisher Exact Tests were performed for continuation or discontinuation of PPI at 3 months after anti-reflux surgery. Cox Proportional Hazards Regression Analysis and Kaplan-Meier Estimates were utilized. Statistical significance was defined as $p < 0.10$ given the small sample size.
- The primary endpoint was discontinuation of PPI. The secondary endpoint was restarting of PPI.

## CONCLUSIONS

- In this multi-center retrospective cohort study, we found increasing BMI, class II obesity of higher, and a fundoplication alone were the strongest predictors for needing to restart a PPI after anti-reflux surgery in patients with HH.
- Failure of the fundoplication due to increasing body mass causing increased intrathoracic pressure may explain this finding.

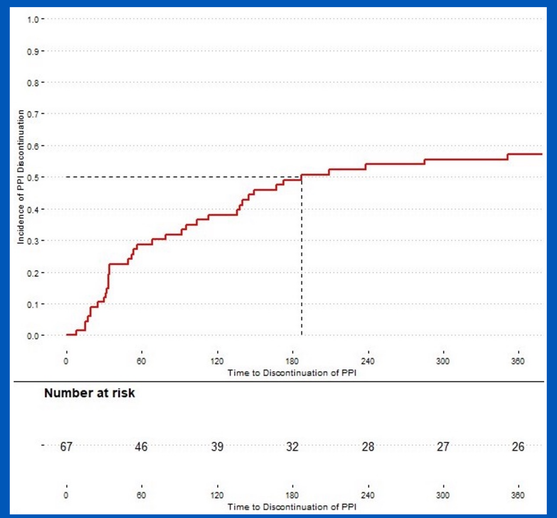


# Every 5-point increase in BMI is associated with a 20% increased risk of restarting PPI after anti-reflux surgery in patients with hiatal hernia.

**Table 1:** Baseline Characteristics of All Patients by Discontinuation of PPI at 3 months and Unadjusted Cox Proportional Hazards Regression Analysis for Discontinuation and Restarting of PPI in Patients with Hiatal Hernia After Anti-Reflux Surgery

| | Unadjusted Univariable Analysis | | | Unadjusted Cox Proportional Hazards Regression | | | |
|---|---|---|---|---|---|---|---|
| | Median (IQR) or Fraction (%) | | | Discontinuation of PPI | | Restarting of PPI | |
| | PPI Continued At 3 months N=39 | PPI Discontinued At 3 months N=28 | P value | HR (95% CI) | P value | HR (95% CI) | P value |
| Age at Surgery, per 10 years | 69.0 (60.5-75.9) | 63.3 (59.0-69.7) | 0.12 | 0.83 (0.65-1.07) | 0.15 | 0.80 (0.54-1.17) | 0.25 |
| Male | 10 (25.6%) | 6 (21.4%) | 0.78 | 1.03 (0.53-1.98) | 0.94 | 0.44 (0.13-1.50) | 0.19 |
| White race | 39 (100%) | 28 (100%) | NA | NA | NA | NA | NA |
| Hispanic ethnicity | 0 | 0 | NA | NA | NA | NA | NA |
| Height, per 30 cm | 162.6 (156.1-174.5) | 165.6 (163.-172.7) | 0.19 | 1.60 (0.91-3.24) | 0.19 | 0.63 (0.15-2.62) | 0.53 |
| Weight, per 10 kg | 83.9 (69.7-92.2) | 84.0 (73.8-93.2) | 0.55 | 1.06 (0.91-1.24) | 0.46 | 1.03 (0.77-1.38) | 0.83 |
| Body Mass Index, per 5 kg/m$^2$ | 30.7 (26.3-34.7) | 31.2 (28.1-33.1) | 0.83 | 1.09 (0.95-1.24) | 0.22 | 1.20 (1.05-1.37) | **0.0074** |
| • Body Mass Index ≥ 35 kg/m$^2$ | 8 (20.5%) | 4 (14.3%) | 0.75 | 0.81 (0.37-1.73) | 0.58 | 8.45 (2.85-25.06) | **<0.001** |
| Obesity | 22 (56.4%) | 16 (57.1%) | 1.00 | 1.05 (0.58-1.88) | 0.88 | 1.69 (0.68-4.21) | 0.26 |
| Never Smoker | 27 (69.2%) | 13 (46.4%) | **0.079** | 0.77 (0.43-1.38) | 0.38 | 0.81-5.09 | 0.13 |
| Moderate to Severe Alcohol Use | 7 (17.9%) | 9 (32.1%) | 0.25 | 1.20 (0.62-2.32) | 0.59 | 0.34 (0.08-1.46) | 0.15 |
| Type 2 Diabetes | 11 (28.2%) | 3 (10.7%) | 0.13 | 0.64 (0.30-1.37) | 0.25 | 0.69 (0.20-2.36) | 0.55 |
| Interstitial Lung Disease | 9 (23.1%) | 3 (10.7%) | 0.33 | 0.86 (0.41-1.79) | 0.69 | 0.85 (0.28-2.58) | 0.76 |
| History of Aspiration | 2 (5.1%) | 0 | 0.51 | 1.15 (0.28-4.77) | 0.85 | 1.13 (0.15-8.47) | 0.91 |
| **Type of Surgery** | | | | | | | |
| Hiatal Hernia Repair, alone | 7 (17.9%) | 4 (14.3%) | 0.75 | 0.83 (0.48-1.63) | 0.69 | 0.63 (0.15-2.72) | 0.54 |
| • Mesh Utilized | 7 (20.6%) | 8 (36.4%) | 0.23 | 1.44 (0.71-2.91) | 0.32 | 0.51 (0.14-1.82) | 0.30 |
| Fundoplication, alone | 5 (12.8%) | 6 (21.4%) | 0.51 | 1.47 (0.71-3.06) | 0.30 | 2.45 (0.92-6.49) | **0.0722** |
| • Nissen | 27 (84.4%) | 19 (79.2%) | 0.73 | 1.28 (0.53-3.05) | 0.58 | 1.22 (0.28-5.36) | 0.79 |
| • Toupet | 4 (12.5%) | 4 (16.7%) | 0.71 | 0.86 (0.33-2.20 | 0.75 | 0.42 (0.06-3.20) | 0.41 |
| Hiatal Hernia Repair and Fundoplication | 27 (69.2%) | 18 (64.3%) | 0.79 | 0.89 (0.48-1.63) | 0.69 | 0.65 (0.27-1.58) | 0.35 |
| Laparoscopic Approach | 37 (94.9%) | 28 (100%) | 0.51 | 1.00 (0.24-4.14) | 1.00 | 0.69 (0.09-5.19) | 0.72 |
| Estimated Blood Loss, per 20 mL | 25.0 (10.0-30.0) | 20.0 (10.0-30.0) | 0.67 | 1.05 (0.95-1.15) | 0.33 | 1.07 (0.95-1.19) | 0.26 |
| Elapsed Time for Surgery, per 30 minutes | 140.0 (112.8-181.5) | 142.0 (106.0-160.0) | 0.58 | 1.07 (0.86-1.31) | 0.56 | 1.09 (0.85-1.40) | 0.51 |
| • Time ≥ 180 minutes | 6 (30.0%) | 3 (23.1%) | 1.00 | 1.03 (0.40-2.68) | 0.95 | 0.80 (0.21-2.97) | 0.73 |
| **Pre-Surgical Evaluation** | | | | | | | |
| EGD prior to surgery | 26 (66.7%) | 24 (85.7%) | **0.094** | 2.05 (0.99-4.27) | **0.0540** | 0.58 (0.22-1.50) | 0.26 |
| • Esophagitis | 5 (19.2%) | 6 (25.0%) | 0.74 | 1.37 (0.65-2.92) | 0.41 | 1.37 (0.43-4.36) | 0.60 |
| Manometry Performed | 16 (41.0%) | 14 (50.0%) | 0.62 | 1.43 (0.80-2.56) | 0.22 | 0.38 (0.15-0.96) | **0.0407** |
| • Normal Findings | 4 (30.8%) | 5 (38.5%) | 1.00 | 1.45 (0.59-3.54) | 0.42 | 0.71 (0.14-3.67) | 0.68 |
| pH Testing Performed | 15 (38.5%) | 4 (14.3%) | **0.053** | 0.83 (0.43-1.57) | 0.56 | 0.64 (0.24-1.76) | 0.64 |
| • Total Acid Exposure, per 3 % | 8.1 (5.3-14.1) | 9.2 (7.1-11.8) | 0.88 | 1.12 (0.85-1.48) | 0.41 | 0.71 (0.42-1.22) | 0.22 |
| • DeMeester Score, per 5 points | 28.7 (20.5-48.3) | 28.4 (21.4-40.8) | 1.00 | 1.05 (0.92-1.19) | 0.50 | 0.86 (0.21-2.97) | 0.23 |
| Large Hiatal Hernia on Endoscopy | 13 (56.5%) | 12 (57.1%) | 1.00 | 1.04 (0.58-1.87) | 0.90 | 0.54 (0.21-1.40) | 0.21 |
| Large Hiatal Hernia on CT Imaging | 16 (41.0%) | 13 (46.4%) | 0.80 | 1.00 (0.51-1.99) | 0.99 | 0.85 (0.29-2.44) | 0.76 |
| PPI prior to surgery | 37 (94.9%) | 25 (89.3%) | 0.64 | 1.50 (0.47-4.85) | 0.50 | NA | NA |
| **Endpoints** | | | | | | | |
| **All Patients** (N=67, 8 patients discharged not on PPI after surgery) | | | | **Patients with Initial PPI Discontinuation** (N=45) | | | |
| PPI Discontinued at Follow Up | 46/67 (61.3%) | | | PPI Reinitiated at Follow Up | | 21/45 (60.0%) | |
| Median Time Discontinuation of PPI, days | 99.5 (33.0-230.8) | | | Median Time to Reinitiation PPI, days | | 346.0 (183.0-880.0) | |

**Figure 1:** Cumulative Incidence of Discontinuation of PPI in Patients with Hiatal Hernia Following Anti-Reflux Surgery




## RESULTS

- A total of 75 patients were included. Median times to PPI discontinuation and its subsequent restarting were 99.5 (IQR: 33.0-230.8) and 346.0 days (IQR: 183.0-880.0), respectively. **Figure 1.**
- At 3 months after surgery, being a never smoker, having had an upper endoscopy (EGD) or pH testing prior to surgery were associated with the initial discontinuation of PPI at $p<0.10$. Having had an EGD increased the risk of discontinuation of PPI by 105%, p=0.0540. **Table 1.**
- Body mass index (BMI), total percentage of acid exposure time, and DeMeester score were not associated with PPI discontinuation.
- After discontinuation, class II obesity or higher (BMI ≥ 35.0 kg/m$^2$) was very strongly associated with the restarting of PPI, $p<0.001$. Every increase of 5 kg/m$^2$ was associated with a 20% increased risk of needing to restart a PPI after anti-reflux surgery.
- Compared to HHR +/- F, a fundoplication alone increased the risk of restarting a PPI by 145% (HR 2.45, 95% CI: 0.92-6.49, p=0.0722). **Figure 2.**
- Having a large HH prior to surgery was not associated with restarting of PPI.

**Figure 2:** Cumulative Incidence of Restarting PPI by BMI in Patients with Hiatal Hernia Following Surgery