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# Surgical Innovations for GERD: Comparing Outcomes of Magnetic Sphincter Augmentation and Nissen Fundoplication

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# Comparing Outcomes of Magnetic Sphincter Augmentation and Nissen Fundoplication

by

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**Abstract**

Gastroesophageal reflux disease (GERD) is a common chronic upper gastrointestinal disease with both objective and subjective components. It is defined as a reflux of gastric contents into the esophagus, which causes symptoms such as heartburn, regurgitation, and dysphagia. Severity of the disease is dependent on both severity of the symptoms and severity of the mucosal damage done by the reflux. While many cases of GERD can be managed with oral medication, persistent and refractory cases require surgical intervention. The purpose of this literature review is to compare the efficacy of GERD's gold standard surgical technique, the Nissen fundoplication, with a new surgical technique, magnetic sphincter augmentation. Studies were included if they analyzed either procedure against itself or directly compared the two procedures. No specific requirements were set, but special attention was paid to the patient inclusion criteria to assess for common themes between the studies. The data available at this time indicates that in patients who qualify for both procedures, magnetic sphincter augmentation and Nissen fundoplication produce similar levels of efficacy and patient satisfaction.

*Keywords:* DeMeester score, gastroesophageal reflux/diagnosis, gastroesophageal reflux/surgery, GERD, fundoplication, fundoplication/economics, and magnetic sphincter augmentation

## Introduction

Gastroesophageal reflux disease (GERD) is a common chronic upper gastrointestinal disease with both objective and subjective components. GERD can significantly hinder quality of life and increase a patient's risk for esophageal ulceration, esophageal stricture, Barrett's esophagus, and esophageal adenocarcinoma. Dating back to the 1950s, GERD was primarily treated surgically with the Nissen fundoplication, which wraps the fundus of the stomach around the lower esophageal sphincter to reinforce it and cease pathologic refluxate (Allaix, 2014). Later on with the advent of proton pump inhibitors (PPIs), a medication which decreases gastric acid production, rates of surgery greatly declined. However, the Nissen still has its place in the spectrum of treatments for GERD. It serves to this day as the gold-standard surgical option, predominantly for patients experiencing persistent symptoms or disease progression despite maximum pharmacologic therapy. Variations on the Nissen fundoplication, including Toupet and Dor partial fundoplications, are frequently utilized based on esophageal motility and contractility. A new anti-reflux procedure, magnetic sphincter augmentation, was approved by the FDA in 2012. This procedure functions to reinforce and restore competency to the lower esophageal sphincter via a bracelet of magnetic beads (McQuiad, 2019). The purpose of this literature review is to reveal the efficacy of this new surgical technique compared to the gold-standard Nissen fundoplication.

### Statement of the Problem

The first Nissen fundoplication was described in 1955 (Min, 2014) and has stood as the gold standard for anti-reflux surgery since then. Due to its long-standing history, it is a well-known procedure, and there is a plethora of data analyzing its efficacy and indications. With the

recent advent of magnetic sphincter augmentation, there is a smaller but ever-growing quantity of data available analyzing this procedure's place in the spectrum of treatments for GERD.

**Research Question**

In the surgical treatment of GERD, is there a statistical difference in the efficacy of magnetic sphincter augmentation (MSA) versus Nissen fundoplication (NF) for patients who qualify for both procedures?

**Research Methods**

A literature review was performed using the following electronic search databases: PubMed, Clinical Key, and Cochrane Library. Both keyword and MeSH terms (*DeMeester score, gastroesophageal reflux/diagnosis, gastroesophageal reflux/surgery, GERD, fundoplication, fundoplication/economics, and magnetic sphincter augmentation*) were used to define a selection of literature discussing Nissen fundoplication and magnetic sphincter augmentation's utility in the treatment of GERD. More articles than what are listed below were found but excluded due to not being applicable to this review. They were deemed not applicable if they did not directly analyze or compare the two surgeries in question or if the patient population was predominantly or intentionally pediatric.

## Literature Review

A review of the literature reveals efficacy of MSA and NF individually in terms of subjective and objective control of GERD symptoms. This review may also reveal equivalent efficacy profiles of the two surgeries when compared to each other.

## The Pathophysiology of GERD

At the juncture of the esophagus and the stomach, a sphincter of smooth muscle called the lower esophageal sphincter (LES) acts as a selective barrier. In its ideal form, it relaxes to allow food boluses to pass into the stomach from the esophagus and contracts to prevent acidic contents of the stomach from reaching the esophagus. GERD is defined as reflux of gastric contents into the esophagus, which causes symptoms such as heartburn, regurgitation, and dysphagia. It is most commonly due to a weakened or incompetent LES (Allaix, 2014). An incompetent LES is multifactorial. The presence of a hiatal hernia, esophageal hiatus size, esophageal contractility and motility, and esophageal anatomy all contribute to appropriate functioning of this highly dynamic area. GERD severity is a spectrum and is dependent on both subjective severity of the symptoms and objective severity of the mucosal damage inflicted by the reflux. Some individuals have significant symptoms without significant reflux, and some have significant reflux without the same proportion of symptoms. With PPIs and antacids readily available over the counter, it is common for providers and patients to dismiss GERD as a minor annoyance rather than an actual disease, but for patients who experience refractory symptoms or who are at risk for complications from mucosal damage, GERD is a highly intricate disease with multiple factors influencing how it is managed.

## The Complexities of Diagnosing and Surgical Decision Making in GERD

The diagnosis of GERD begins with a thorough history and physical. Once atypical cardiac symptoms and other pathologies (such as H. pylori, gastritis, and more) are ruled out, a diagnosis of GERD can be made clinically. Patients will first trial a course of PPIs to see if medication can control their symptoms. If so, no further investigation into an objective diagnosis of GERD is needed. For patients who do not respond to maximal doses of medication,

experience adverse side effects, or do not wish to remain on lifelong medication, surgery can be indicated, and investigation into more permanent treatment options begins.

Due to the significant subjectivity of this disease, standardized questionnaires are frequently utilized to assess a patient's perceived disease severity and to monitor medical and surgical treatment over time. The Gastroesophageal Reflux Disease-Health Related Quality of Life (GERD-HRQL) questionnaire is a commonly used tool that has been validated as a reliable, practical, and precise assessment of common GERD symptoms (Velanovich, 2007). It consists of ten questions (Table 1) which asks patients to rate their symptoms on a scale of 0 to 5, with 0 being no symptoms and 5 being symptoms are incapacitating to daily activities, plus a non-scored question on how satisfied the patient is with his or her present condition (satisfied, neutral, or dissatisfied). Total scores range from 0 (best possible score) to 50 (worst possible score). The tool does not categorize scores into classifications such as mild, moderate, or severe, but rather requires the provider to interpret severity on an individual basis and what treatment regimen should be selected.

Table 1.

*The Gastroesophageal Reflux Disease-Health Related Quality of Life instrument.*

| |
|---|
| • **Scale**: No symptoms = **0**; Symptoms noticeable, but not bothersome = **1**; Symptoms noticeable and bothersome, but not every day = **2**; Symptoms bothersome every day = **3**; Symptoms affect daily activities = **4**; Symptoms are incapacitating, unable to do daily activities = **5** |
| • **Questions** |
| __ 1. How bad is your heartburn? 0 1 2 3 4 5 |
| __ 2. Heartburn when lying down? 0 1 2 3 4 5 |
| __ 3. Heartburn when standing up? 0 1 2 3 4 5 |
| __ 4. Heartburn after meals? 0 1 2 3 4 5 |
| __ 5. Does heartburn change your diet? 0 1 2 3 4 5 |
| __ 6. Does heartburn wake you from sleep? 0 1 2 3 4 5 |
| __ 7. Do you have difficulty swallowing? 0 1 2 3 4 5 |
| __ 8. Do you have pain with swallowing? 0 1 2 3 4 5 |
| __ 9. Do you have bloating or gassy feelings? 0 1 2 3 4 5 |
| __ 10. If you take medication, does this affect your daily life? 0 1 2 3 4 5 |
| __ How satisfied are you with your present condition? Satisfied __ Neutral __ Dissatisfied __ |

For surgery to be indicated, an objective diagnosis of GERD must be made. In order to determine this, a patient must undergo a barium swallow, esophagogastroduodenoscopy (EGD), esophageal manometry, and pH monitoring, as defined by Worrell et. al. (2014) in their literature

review of surgical decision making for GERD. This cohort of diagnostics functions to ensure that a patient's symptoms are not being caused by other pathologies and to assess the competency of his or her esophagus to determine appropriate procedure selection.

Esophageal mucosa and the damage caused by gastric reflux can be directly visualized on EGD. Surgeons most commonly determine the extent of damage using the Los Angeles Classification System for Esophagitis (Table 2). First published in 1999, this system has been validated in multiple studies highlighted in the article by Sami and Ragunath (2012) as a consistent grading system for predicting outcomes of acid reflux therapy. The presence and extent of mucosal damage objectively diagnoses and stratifies severity of GERD.

Table 2.

*The Los Angeles Classification of Esophagitis*

| | |
|---|---|
| **Grade A** | One (or more) mucosal break no longer than 5 mm that does not extend between the tops of two mucosal folds |
| **Grade B** | One (or more) mucosal break more than 5 mm long that does not extend between the tops of two mucosal folds |
| **Grade C** | One (or more) mucosal break that is continuous between the tops of two or more mucosal folds but which involve less than 75% of the circumference |
| **Grade D** | One (or more) mucosal break which involves at least 75% of the esophageal circumference |

Further contributing to the objective diagnosis of GERD is the DeMeester score, which is calculated during esophageal pH testing. During this procedure (which is usually conducted in conjunction with an EGD), a pH probe is endoscopically placed at the LES to monitor the frequency and duration of acid reflux episodes for a length of time (generally 24-48 hours.) Using the total number of reflux episodes in 24 hours, the percentage of total time that esophageal pH is < 4, the percentages of upright and supine time with an esophageal pH < 4, the number of reflux episodes lasting longer than 5 minutes, and the length of the longest episode of reflux in minutes, the DeMeester score is calculated (Table 3). A composite score of 14.7 or less is considered normal, or GERD negative. A score higher is considered abnormal, or GERD

positive, and the higher the score, the more severe the disease. According to Neto et. al. (2019), the DeMeester score equation has a proven sensitivity of 96%, specificity of 100%, and accuracy of 98% compared to just monitoring acid exposure time, which has a sensitivity, specificity, and accuracy of 96%. And while this article reveals that the DeMeester score correlates with esophagitis severity, hiatal hernia size, abnormal esophageal motility, and the incompetency of the LES, the calculation alone is limited by an inability to correlate reflux episodes with reflux symptoms. For this, pH testing includes a subjective component. For the 24-48 hours that the pH probe is in place, patients wear a symptom monitor to record the timing, duration, and type of symptoms. At the end of the test, providers skilled in esophageal pH analysis correlate the pH readings, the DeMeester score, and symptoms to determine if GERD is the cause of the patient's symptoms.

Table 3.

*Parameters used in the derivation of DeMeester scores based on 24-hour pH monitoring*

| Parameters | Asymptomatic controls ($n = 15$) | Normal value |
|---|---|---|
| Recumbent period | 0.286% ± 0.467 | <1.2% |
| Total period | 1.478% ± 1.381 | <4.2% |
| No. episodes > 5 min | 0.6 ± 1.241 | 3 or less |
| Longest episode | 3.866 min ± 2.689 | <9.2 min |
| Upright period | 2.33% ± 1.975 | <6.3% |
| No. total episodes | 20.6 ± 14.773 | <50 |

Once GERD is objectively diagnosed, a surgical technique can be selected. The 2014 literature review by Worrell et. al. mentioned earlier created an algorithm outlining proper surgical selection based on parameters found in diagnostic testing (Figure 1). According to the authors, for patients with normal esophageal function, an NF or MSA can be indicated, but an NF is preferred if the patient has a hiatal hernia larger than 3 cm. The authors do not disclose how they determined the hernia size cut-off. The authors highlight the infancy of MSA and recognize the need for further studies at the time of this article's publishing to adequately stratify

where MSA lands in the spectrum of treatments for GERD. The articles below and the discussion following investigate this.

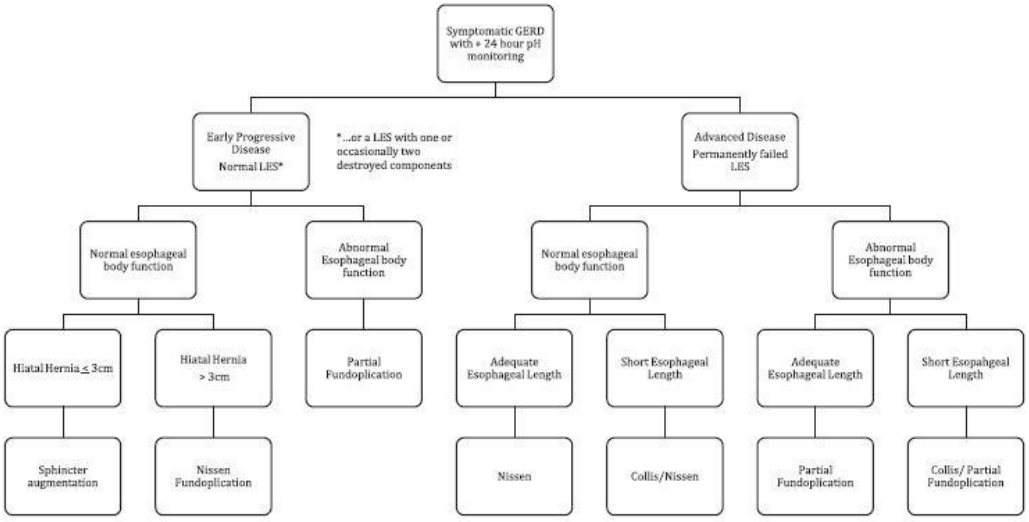


*Figure 1.* Algorithm of surgical treatment options.

## Surgical Management of GERD

### The Efficacy of the Nissen Fundoplication

The following articles highlight the efficacy of the Nissen fundoplication (NF) over time to reveal why it has persisted as the anti-reflux surgery gold standard. Among its numerous strengths is its ability to eliminate heartburn symptoms, decrease esophageal acid exposure, and improve LES pressure, which is proven in a randomized control trial conducted by Anvari et. al. (2011) This study, composed of 101 participants split 1:1, compared optimized PPI therapy to NF for the treatment of GERD in patients who were stable and symptomatically controlled with long-term medical therapy over three years. Inclusion criteria included men or women ages 18-70 treating their GERD adequately with long-term PPI therapy for a minimum of one year and expected future duration of at least two years, a normal GERD Symptom Score (GERSS)

(similar to the GERD-HRQL) and a normal Global Visual Analog Scale (VAS) while on medication, and the percentage of acid reflux in 24 hours > 4% off medication on pH studies.

Results of the study revealed that both medication and surgery decreased symptom questionnaires in patients, but there was no statistical difference between the two treatment modalities. There was a statistical difference between the number of heartburn-free days. Surgical intervention produced a mean of 1.35 more heartburn-free days per week compared to medical therapy, with surgery giving patients 6.81 ± 0.66 days and medical therapy giving patients 5.98 ± 1.82 days (95% confidence interval (CI) 0.36-2.35, p = 0.0077). There was a significant improvement in esophageal acid exposure time (determined by the percentage of time with pH < 4 on pH testing) for both groups (10.26 ± 11.61% to 2.11 ± 3.84% for surgical and 9.46 ± 5.70% to 4.29 ± 6.66% for medical), but there was not a statistical difference between the two. At three years, the surgical group had a significantly better LES pressure than the medical group, with a mean difference of -5.85 (95% CI, -8.84 - -2.85, p = 0.0002). Since one of the eligibility requirements for this study was symptomatic control on PPIs as indicated by a VAS score > 70, medical patients maintained their symptom control over three years (82.60 ± 10.79 at baseline to 81.95 ± 14.25), whereas surgery showed a statistically significant improvement, with VAS scores increasing from a mean of 81.79 ± 12.59 to 92.67 ± 11.49 (p = 0.0072). The mean difference between the two groups was -10.16 (95% CI, -17.82, -2.51, p = 0.0093).

Limitations of the study include the small sample size due to the strict inclusion requirements, especially the requirement that symptoms must be well-controlled on PPIs. There are conflicting schools of thought on if patients need to be well-controlled or not on reflux medication to predict successful surgical outcomes. By excluding patients uncontrolled on medication, surgical efficacy was only able to be assessed on patients who respond. Regardless,

due to sample size there was an inability to measure a statistical difference between the groups in certain parameters, including LES pressure and esophageal acid exposure time. There was a significant improvement in this parameter for the surgical group, and surgery led to normalization of this measurement, whereas medical therapy did not. With a larger sample size, a statistical difference could possibly be revealed. One of the benefits of this study was the detailed follow-up they did on patients with treatment failures. Showing that those who failed initial treatment would commonly proceed to fail repeated treatments highlights the complex nature of GERD, and one could possibly infer that there are unknown components that contribute to GERD that may not be able to be identified on routine testing. Regardless of the limitations, this study establishes NF as an effective surgical option for objectively controlling GERD long-term.

Despite the success of NF highlighted above, NF's reputation of adverse side effects has historically clouded its efficacy among the general population, with many thinking experiencing an incapacitating inability to belch or vomit after the procedure is worse than the symptoms that led them to the procedure in the first place. The article by DeMeester et. al. (1986) evaluated the results of 100 consecutive Nissen fundoplications performed by DeMeester at his practice. The patients all had objective GERD as determined by a composite score created and validated by the authors on abnormal 24-hour esophageal pH monitoring (this will later be titled the DeMeester score), no evidence of esophageal stricture or other anatomic abnormalities, and normal esophageal motility. The goals of this study were to advance the authors' understanding of patient selection and operative technique and how those factors can impact side effects of the surgery brought up by other studies. They evaluated patient outcomes annually for 10 years post-operation. Patients were evaluated using a standardized GERD questionnaire which asked about

recurrences of heartburn, regurgitation, aspiration, inability to belch or vomit, dysphagia, the need for a dilatation, increased flatus, and symptomatic gas bloat.

Of the 100 patients, none died from surgery. Three symptomatic recurrences of GERD occurred at 6 months, 2 years, and 7 years. There were 36 patients, including two of the three with symptomatic recurrences of GERD, who underwent repeat pH studies. Of these, six had abnormal results. Using this information and the annual questionnaire data collected, an actuarial analysis was performed and determined that the operation had a 91% success rate in controlling reflux symptoms for up to 10 years. They surmised that long-term symptom control can be achieved by NF when patient selection is based on the presence of reflux symptoms, an abnormal pH study, and normal esophageal motility. They determined that side effects such as symptomatic gas bloat and inability to belch often had to do with gastric rather than esophageal pathology. DeMeester et. al. (1986) were also able to decrease operation side effects through surgical advancements such as using a larger bougie and creating a shorter and narrower fundic wrap.

The limitations of this study include the small number of participants who underwent repeat pH studies and the inherent subjectivity of the questionnaires. And while actuarial analysis reported 10-year results, the average follow-up time period of the cohort was only 45 months. A study assessing patient satisfaction and outcomes at a true 10-year interval for all patients should be performed. Despite that, this article still highlights the overall success of the procedure over a longer period of time and also discovers technical improvements that have improved outcomes and decreased side effects, which have historically influenced the reputation of this procedure. The author and this study has been referenced in many pieces of literature as key players in formulating the success of anti-reflux surgery.

The next article by Lafullarde et. al. (2001) reports 5-year outcomes of NF from a single university teaching hospital. Similar to DeMeester's article, the authors' goal was to determine if NF produced sustained reflux control. However, this study's goals focused on subjective control. An independent investigator contacted the 178 patients enrolled in the study and used a standardized and structured questionnaire to collect data. Of those, 166 patients responded with follow-up ranging from 5 to 8 years post-operation (median 6 years). Patients qualified if they had documented esophagitis on EGD or an abnormal pH study. Patients were not excluded from the surgery based on BMI, hiatal hernia presence or size, prior abdominal surgery history, or esophageal strictures.

The questionnaire used to collect data graded the following symptoms on a scale of 0 to 10, with 0 being no symptoms and 10 being severe symptoms: heartburn, dysphagia to solids or liquids, bloating, ability to belch, ability to relieve abdominal distension, ability to eat a normal diet, whether the respondent would undergo the same procedure again under similar circumstances, and overall satisfaction with the procedure. Adverse events and surgical revision rates were also collected. Data analysis of the collected information was performed on an intention-to-treat basis and included patients whose original surgery was converted from laparoscopic to open (n=21) and patients who had surgical revisions (n=27).

Of the 166 respondents, 100 patients reported no heartburn, and 45 had only occasional episodes of minor heartburn, defined as a score of 3 or less on the standardized questionnaire. There were 15 patients who reported a heartburn score of 4-6 (moderate), and six patients graded it 7 or higher, which is defined as severe. Most patients reported a heartburn score of 7 or higher before surgery. Therefore, 87% of patients were considered free of significant reflux symptoms at the latest follow-up period. There were 18 patients reported returning to regular acid

suppression medication for reflux symptoms. More patients reported severe (grade of 7-10 on questionnaire) liquid dysphagia before surgery than after surgery, however, the incidence of mild (grade 1-3) and moderate (grade 4-6) liquid dysphagia increased in the respondent pool ($p < 0.001$, $\chi^2$ test). Similar results were seen with solid food dysphagia ($p < 0.001$, $\chi^2$ test) (Figure 2). In the cohort, 72% of patients claimed they were able to belch. A reported 66% of patients experienced occasional epigastric bloating, but 71% of them were able to relieve the discomfort with belching. Overall, patient satisfaction with the procedure produced a mean score of 8.2 out of 10. Of the entire study population, 90% of patients reported they would repeat this operation in similar circumstances.

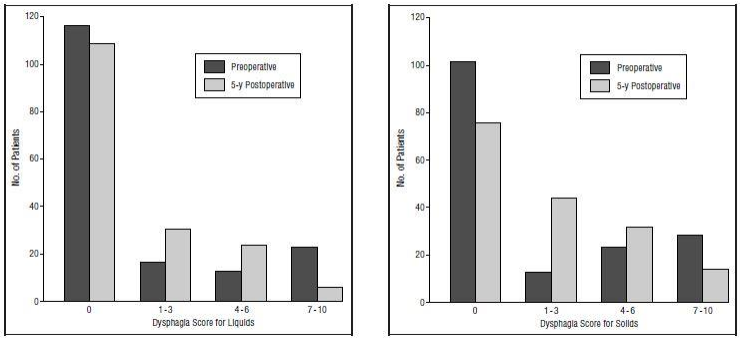


*Figure 2.* Chi square test results for liquid and solid dysphagia.

Despite subjective success being the goal of the study (Lafullarde, 2001), subjective measures of follow-up limit the validity of the research without objective counterparts. Some patients within the study's cohort underwent post-operative endoscopy, manometry, and pH testing, but it was only for symptom recurrence, adverse effects, or for surgical revision. The authors explain that some patients may experience subjective symptoms without objective reflux, and some patients may have objective reflux without any symptoms, and therefore, the true marker of success of the procedure for this study should be the subjective patient satisfaction. This highlights the complicated nature of surgical decision-making for GERD as there are many

subjective and objective variables. Regardless, objective evidence of the efficacy of the surgery could strengthen this study. One benefit of this study was the authors' choice to include patients who required a conversion to an open fundoplication. Since these patients would likely be less satisfied with the outcome of their procedure, the authors avoided bias and artificially high satisfaction rates by including them. The key benefit of this study for this scholarly project was the lack of patient exclusion criteria it used, as overall positive results were reported across a wide range of patient profiles. This reinforces the strength and wide utility this procedure has in the spectrum of GERD treatment.

The next study by Prassas et. al. (2017) investigates long-term outcomes of NF in patients who underwent the surgery in a low-volume community hospital setting through a retrospective analysis. Up to this point in this paper, all articles were conducted at a surgical center, gastroenterology center, or by foregut surgeons. The goals of this article aim to reveal if the success of the surgery can be replicated in a low-volume hospital with general surgeons. From 1997 to 2012, 376 patients underwent the procedure performed by a single surgeon at the facility. All patients had normal esophageal motility. No other patient inclusion or exclusion criteria were documented. Subjective symptoms were assessed pre- and post-operatively using a 10-point Likert scale of how satisfied or unsatisfied a patient is with their current medical condition using a subjective grading scale. Primary outcomes include the post-operative Likert scale results, a quality of life assessment using the measurements of if the respondent's quality of life is 'worse', 'same as before', 'better', or 'much better' after the surgery, and inquiries about return to use of PPIs and revisional surgery.

Of the 376 patients, 166 responded to the study's questionnaire sent via mail, and the median follow-up time was 8.8 years post-operation (range 1.4-17 years). Results of the

questionnaire are as follows: 129/166 (77.7%) reported a complete resolution of heartburn, defined as a maximum of one episode of heartburn weekly, 15/166 (9%) experienced more than once weekly episodes of heartburn, and 19/166 (11.4%) experienced daily heartburn. Of the 166 respondents, 51 patients had dysphagia pre-operatively, and 29/51 (56.8%) reported resolution of that symptom post-operatively. Of the remaining 115 who reported no pre-operative dysphagia, 31 respondents (18.6%) reported a new-onset dysphagia, for a total of 53 of the 166 respondents (31.9%) experiencing dysphagia after NF. Of the 166, 57 (34.3%) reported regurgitation post-operatively, and 34 (20.4%) experienced it on a daily basis. There were 102 respondents (61.4%) who reported increased bloating after surgery. There were 44 patients (27%) who reported a decreased ability to belch or vomit. There were 38 patients (22.9%) who reported still using PPIs after surgery, and 10 (6%) had undergone a revision. Despite this, 120/166 (73.6%) reported a subjective improvement in their quality of life, and 138/166 (85%) would undergo the surgery again in similar circumstances.

Limitations to this study include a small number of respondents (166/376) which can severely skew data, the lack of a control group, the lack of a standardized tool to assess quality of life, and the lack of inclusion of objective evaluation of the respondents' resolution of GERD. Using only descriptive statistics is also a limitation. A benefit of this study was the use of standardized surgical technique. Over the 15-year time span, the same surgeon performed the same surgery for all respondents, which has not always been the case with other studies reviewed. This eliminated any intraoperative variables. The overall positive long-term outcomes of this study establishes the lasting efficacy of this procedure and its efficacy when being performed in community hospitals, not just specialized centers, which can be difficult to gain access to in rural and lower population areas.

The last article in this scholarly project evaluating the efficacy of NF is a report of 20-year outcomes by Robinson et. al (2014). The aim of their study was to determine symptomatic success over an extended period of time through a 5-point validated GERD questionnaire (Table 4) for heartburn, regurgitation, and dysphagia, as well as return to PPI and surgical revision rates.

Table 4.

*Symptom scale for 5-point GERD questionnaire*

| Score | Frequency |
|---|---|
| 0 | Never |
| 1 | Rare |
| 2 | Occasional |
| 3 | Daily |
| 4 | Continuous |

They identified 193 patients in their selected time frame and contacted them via telephone. A standardized script created by the authors was used to deploy the surveys. There were 51 respondents between the ages of 27 and 70 at the time of the surgery who completed the survey (100 were unable to be reached, 40 were deceased, and two refused to respond.) The respondents had a median post-surgical time of 19.7 years.

Off the 51 participants, 38 reported complete control of heartburn and regurgitation at 20 years. An additional ten patients reported less than one heartburn episode per week. Three patients reported both heartburn and regurgitation, and no patients reported just regurgitation. There were 24 patients who reported dysphagia, but only eight reported having the symptom daily. 78% of the cohort had additional gastrointestinal conditions. There were 11 respondents had a completely negative symptom questionnaire. There were 22 respondents using PPIs at 20 years. Nine of 51 had a surgical revision during the study's time period, and seven of those had complete resolution of symptoms after the re-do. There was one patient underwent multiple revisions. Of the nine who had revisions, eight of them reported the highest satisfaction rating on

the questionnaire. Overall, 46 of 51 reported being satisfied with their choice of surgery, with 39 of them giving the highest satisfaction rating on the questionnaire.

Limitations of this study include a small sample size, purely subjective responses as the results, and only descriptive statistics being utilized. A similar length study should be performed including objective testing, such as esophageal pH monitoring or manometry. Additionally, a similar length study of a more recent time frame should also be performed, as laparoscopic anti-reflux techniques have evolved since the 1990s. Nonetheless, this article reveals the remarkable durability of NF, which is important for this research question in establishing the surgery's lasting efficacy and its place as a mainstay in the surgical treatment of GERD.

**The Efficacy of Magnetic Sphincter Augmentation**

Magnetic sphincter augmentation (MSA) is a much newer procedure compared to NF. The procedure received FDA approval in 2012 from the year two results of this five-year study conducted by Ganz et. al (2016). The articles publishing the results of year three and five were included in this scholarly project. Ganz et. al. followed 100 adults who underwent MSA at 14 different surgical centers in the US (13 centers) and the Netherlands (one center). Patients were eligible if they were 18-75 years old, had over a 6-month history of GERD, partially responded to daily PPIs, and had pathologic esophageal acid exposure on pH monitoring. Patients were excluded if they had a metal allergy, esophagitis of grade C or D by Los Angeles criteria, a BMI >35, Barrett's esophagus, or impaired esophageal motility. Patients completed a GERD-HRQL questionnaire pre-operatively both on and off PPIs and post-operatively. Primary endpoints included normalization of esophageal acid exposure (<4.5% of time with a pH <4 over a 24-hour period) or a 50% or greater decrease in acid exposure. Secondary outcomes included a 50% or greater improvement in GERD-HRQL scores and a 50% or more reduction in PPI. For each

endpoint, the study defined treatment as successful if the outcome was achieved in at least 60% of the cohort. All results were performed with an intention-to-treat analysis, and patients who were lost to follow-up or had missing data were counted as treatment failures.

The three year results are as follows. There were 64 patients (64%, 95% CI 54-73) who achieved the primary endpoints of normalization or a 50% or greater reduction in esophageal acid exposure. Without intention-to-treat analysis, 64 of the 96 (67%) reached the primary endpoint. The median percentage of time with a pH <4 was 10.9% preoperatively, and it decreased to 3.3% postoperatively ($p < 0.001$). A post hoc analysis was performed for the secondary outcomes and showed that 73% of the cohort had a decrease of 50% or more in GERD-HRQL scores at one year. The median total score pre-operatively was 27 off PPIs and 11 on PPIs, and the median score decreased to 2 without PPIs for the next 3 years ($p < 0.005$). 86% (86/100) of patients had completely stopped using PPIs at one year, 87% (78/90) at two years, and 87% (72/83) at three years ($p < 0.001$) for all three statistics. At 3 years, 13% of patients were regularly taking PPIs, but reported taking them at reduced frequencies. Six patients in the cohort had the device removed in the first 3 years. This was most commonly due to persistent dysphagia. Three of the six had NFs performed after, and their dysphagia resolved. No device erosions or migrations occurred.

At five years, 85 patients completed the follow-up questionnaires. One follow-up was only partially completed and was included on certain analyses and excluded on others. There were 82 patients who completed the follow-up questionnaires and endoscopy. Of the 84, 70 complete questionnaire respondents (83%) still had a 50% or greater reduction in GERD-HRQL scores (95% CI 73-91). 76 of 85 respondents (89.4%) had a 50% or greater reduction in average daily PPI usage (95% CI 81-95), 75.3% responded with a complete cessation of PPI usage, and

9.4% responded only using them on an as-needed basis. The median GERD-HRQL score decreased from 27 without PPIs and 11 with PPIs at baseline to 4 without PPIs at 5 years post-surgery. This is an increase from 2 at 3 years post-surgery but is still within normal range. No device erosions or migrations occurred between 3 and 5 years. An additional device removal occurred between 3 and 5 years due to persistent dysphagia, bringing the total number of devices removed in the study to seven (7% removal rate). All device removals were elective operations and were not due to surgery-related complications.

Despite this study being FDA-approval caliber, its results are still limited by the small sample size and short-term follow-up and could be improved by both a larger sample size and longer-term follow-up. Additionally, esophageal pH testing and manometry were not performed at 3 or 5 years per the FDA-approved and designed protocol. While the 1-year pH results show successful normalization of esophageal acid exposure, 5-year data of this parameter would greatly strengthen the evidence supporting MSA's efficacy in this study by adding more objective data. Using intention-to-treat analyses was a benefit to this study as it allowed for a more clinically realistic statistical analysis, which is crucial in the evaluation of a new treatment option. The consistency in subjective results at 5 years indicate MSA has long-term safety and efficacy for the treatment of GERD, which is why it is significant to this research question.

A randomized control trial by Bell et. al. (2015) was conducted to reveal MSA's efficacy against double-dose PPIs. Patients were recruited from 21 U.S. surgical clinics between July 2015 and February 2017 and were deemed eligible if they were over 21 years old, scored moderate-to-severe regurgitation based on the standardized Foregut Symptom Questionnaire (FSQ), were taking single-dose PPIs for at least eight weeks prior to enrollment, had a BMI <35, had an abnormal DeMeester score, had a normal esophageal manometry, a hiatal hernia of ≤ 3

cm on endoscopy, and did not have Barrett's esophagus or Los Angeles classification grade C or D esophagitis. Eligible patients then also completed additional baseline quality of life questionnaires including the Reflux Disease Questionnaire (RDQ) and GERD-HRQL. They reported results of their studies at six months and one year. The primary endpoint of this study at six months was elimination of regurgitation as measured by the FSQ. Secondary endpoints included a change from baseline as measured by the GERD-HRQL and RDQ, a decrease of ≥ 50% in GERD-HRQL, decrease in esophageal acid exposure, and PPI usage. The primary endpoint at one year was elimination of regurgitation as measured by the same quality of life questionnaires used at six months, as well as EGD and pH monitoring.

There were 152 eligible participants who were divided 2:1 to either twice-daily PPI (BID PPI) therapy (n=102) with 20 mg omeprazole or MSA (n=50). The cohort was evaluated at 6 months with repeat FSQ, RDQ, GERD-HRQL questionnaires and 24-hour pH testing. The PPI group was evaluated on medication, and the surgical group was evaluated without PPI therapy. pH testing was evaluated by a blinded, independent laboratory.

At six months, 42 of 47 respondents (89%) in the surgical cohort achieved resolution of regurgitation compared to 10 of 101 (10%) of the PPI patients ($p < 0.001$), however it is important to mention again that the patient cohort was divided 2:1. When analyzed with ITT, 42 of 50 (84%) of MSA and 10 of 102 (10%) of PPI patients met the primary endpoint ($p < 0.001$). For surgical patients, the average GERD-HRQL score, which scores symptoms 0 to 50 with >20 being severe and <6 as minimal, decreased from 24 at baseline to 6 at six months post-MSA without returning to PPIs. PPI patients decreased from 25 to 24, which reveals a significant difference between the two groups ($p < .002$). RDQ scores, which scores 0 (no regurgitation) to 5 (severe regurgitation) improved from a mean of 4.2 to 1.6 for surgical patients, whereas the PPI

group scores decreased 4.4 to 4.3. A ≥50% improvement in GERD-HRQL scores occurred for 81% of surgical patients and 8% of PPI patients ($p < 0.001$). There were 38 of the 47 surgical patients who reported satisfaction with their treatment compared to 2 of 87 patients in the PPI group. Of the 47 patients who received surgery, 43 had discontinued PPI use at six months. At six months, 44 of the 47 surgical patients and 79 of the 87 PPI patients had pH testing performed. The testing revealed that surgery controlled the number of reflux symptom episodes better than PPIs (22.5 episodes, IQR [13.0-40.5] with MSA and 49.0 episodes, IQR [31.0-76.78] with PPIs ($p < 0.001$)), as well as esophageal acid exposure time with a pH < 4 (39/44 surgery patients and 59/79 PPI patients).

After six months, the study design had patients cross over into other groups to further assess MSA efficacy. Patients from the BID PPI group were allowed to cross over and receive an MSA (MSA crossover cohort) if both their regurgitation symptoms persisted and pH studies demonstrated persistent and excess reflux (defined as 57+ reflux episodes in 24 hours, regardless of pH) despite the PPI usage. Of the 79 patients in the original BID PPI therapy group who completed the six month follow-up testing, 31 met MSA crossover criteria. The remaining 48 did not qualify and were placed on 20 mg once daily omeprazole (called the step-down cohort.) Individual results of the original MSA, crossover MSA, and step-down PPI groups were then reported as one year results.

In the MSA crossover cohort at completion of the study (Bell, 2015), 94% (29 of 31) experienced relief of their moderate-to-severe regurgitation, and 68% (21 of 31) had complete elimination. RDQ scores of the questions specific to regurgitation, with scores of 0 (none) to 5 (severe) improved from 4 (IQR 3.25-4.75) off PPIs and 3.5 (IQR 2.5-4) on PPIs at baseline to 0 (IQR 0-1.25) with MSA ($p < 0.001$). GERD-HRQL scores, which scores symptoms 0 to 50 with

>20 being severe and <6 being minimal, improved from 26 (IQR 21-30) off PPIs and 21 (IQR 18-27) on PPIs at baseline to 4 (IQR 1-7) after surgery ($p < 0.001$). A ≥50% improvement in GERD-HRQL scores was seen in 80.6% of patients (25 of 31). On pH studies, the median DeMeester score (normal < 14.7) improved from 31.7 (IQR 25.2-36.8) to 6 (IQR 2.2-17.6) ($p < 0.001$). 70% (21 of 31) of the cohort scored a normal DeMeester score at 6 months. Similarly, at 12 months, 98% (43 of 44) of the original MSA cohort complete resolution of moderate to severe regurgitation. Median RDQ scores were 0 (IQR 0-0.5). Median GERD-HRQL scores were 5 ($p < 0.001$). A ≥50% improvement of GERD-HRQL scores were seen in 96% (42 of 44) at 12 months ($p < 0.001$). For all MSA patients combined, 91% (68 of 75) had not returned to PPIs at the completion of the study. Median total esophageal acid exposure time improved from 11.5% (IQR 7.9-14.8%) to 1.3% (IQR 0.2-5.3%) ($p < 0.001$), and DeMeester scores improved from 40.5 (IQR 25.7-49.5) to 5.3 (IQR 1.2-18.5). For the step-down cohort, 17% (8 of 48) reported complete regurgitation resolution. RDQ and GERD-HRQL scores did not change significantly from baseline. The median DeMeester score remained elevated at 16.7, however, the pool had a high IQR of 1.9-164, and the score was normal in 54%.

Limitations of this study include a limited follow-up time, small population size, using subjective questionnaires as end points (although pH monitoring does provide objectivity), potential referral bias as the study's patients were recruited from surgical clinics (this was addressed and attempted to be minimized through the use of multiple standardized questionnaires used in surgical and medical clinics alike), and the use of 20 mg omeprazole BID (the U.S. FDA recommended adult dose) instead of 40 mg omeprazole BID (the commonly used adult dose for refractory GERD, but that has no demonstrated superiority in gastric acid control). The limitation on follow-up time is a downfall in terms of gathering data on the long-term efficacy of MSA,

which is highly necessary, although this article does allude to other studies showing no decrease in efficacy between 1 and 5 years. Longer studies need to be performed to assess long-term efficacy. Additionally, descriptive statistics were the only statistics utilized. Some of the results may have benefited from inference statistics to further investigate significance. In addition, patient compliance was not explicitly monitored in the study, as the patients recruited were already familiar in taking daily GERD-suppression medication. This study was also sponsored by Torax Medical, Inc., the company that designed MSA, however, the thorough and objective inclusion criteria does support an overall non-biased study. Overall, considering the results of this study indicate that PPI therapy does not improve over time, longer follow-up time comparing surgical and medical therapies is not necessary. This study reveals the ability of MSA to control regurgitation symptoms sustainably for one year and, more importantly, that it is effective for patients who experienced no response to previous medication therapy.

In the last article of this section, Bonavina et. al. (2013) conducted a study similar in structure to the DeMeester article earlier (DeMeester, 1986). The authors summarized the results of 100 consecutive cases of MSA at their medical institution to provide insight into a practice's long-term experience with the surgery. They report device efficacy, safety, esophageal pH measurements, symptom scores (using the GERD-HRQL and a study-designed questionnaire [Figure 3]), and PPI usage annually.

Patients 1-30 were selected as part of a multicenter pilot study for the procedure. The selection criteria for these patients were 18+ years of age, BMI < 35, GERD symptoms for at least six months, persistent reflux symptoms despite PPI use, reflux confirmed on pH monitoring, and no Barrett's esophagus, motility disorders, anatomic abnormalities, or a known metal allergy. Patients were excluded from the study if they had a hiatal hernia three or more cm

in size or had erosive esophagitis Los Angeles classification grade B, C, or D. The same applied to patients 31-70, but they loosened selection criteria by including patients with hiatal hernias up to three cm, as well as those with grade B esophagitis. Additionally, if patients had <70% effective swallows or a distal amplitude of <35 mmHg on manometry, they were excluded.

1. Why did you decide to undergo surgery?
2. Where did you learn about LINX, who sent you to us?
3. Would you undergo the operation again?
4. Would you recommend it to a friend? and
5. What have you heard about Nissen fundoplication?

*Figure 3.* Study-designed questionnaire

A note from the author: LINX is a brand name for MSA.

Regarding safety and efficacy of the procedure, over the 6 years of the clinical trial, no device erosions or migrations occurred. Of the 100 procedures, three had the device removed. One was for persistent odynophagia, where the patient had a Dor fundoplication performed and the odynophagia resolved. This indicates the patient may not have had enough esophageal motility or strength to open the magnetic device, as the Dor is a partial fundic wrap that requires lower pressure to open. The second patient had theirs removed for persistent GERD symptoms, which resolved with a Toupet fundoplication, which is a larger wrap than the aforementioned Dor, but is still a partial and lower pressure fundic wrap. Of note, this patient had a 3-cm hiatal hernia which was not repaired during the MSA procedure. This highlights the fact that multiple factors, including the presence of hiatal hernias, regardless of size, may contribute to acid reflux, and may not be able to be treated with MSA alone. The third patient's MSA was removed due to persistent dysphagia despite esophageal dilation. The study reports that the patient underwent an Angle of His reconstruction and a Lortat-Jacob procedure, which resolved the symptoms. The study did not go into detail of the exact surgical techniques performed to reconstruct the angle.

Even though in order to be evaluated for anti-reflux surgery, a barium swallow and endoscopy are performed, an anatomic abnormality could have been the issue for this patient. This was not reported in the study, therefore, it is just an inference by this literature review's author, but further highlights the multitude of variables that contribute to GERD.

Surgeries were performed over the course of six years, and the median implant duration at the time this study was reported was three years. 95% of the data collected from patients was at least one year post-surgery. At baseline, median GERD-HRQL scores were 24 off PPIs, and 16 on PPIs. Post-surgery, the median score was 2 (n=95). Median heartburn-specific GERD-HRQL scores decreased from 15 to 2. 87% (83 of 95) reported satisfaction with their current health condition. 85% (81 of 95) reported completely discontinuing PPIs since surgery. When looking at the data in chronological order (the order the patients received the surgery), GERD-HRQL scores and PPI use were comparable.

Esophageal pH monitoring after implantation was only completed on the first 30 patients as a part of the pilot study. The mean follow-up time was 4.2 years. Overall, median DeMeester scores improved from 30.1 (range 15.0-123.3) to 11.2 (1.8-54.9) ($p < 0.001$). Normalization of pH, which is defined as a total percent time with $pH < 4$ for 4.5% or less of the time, occurred in 67% (20 of 30), but an additional 5 patients achieved a reduction of 50% or more of acid exposure time.

Highlights of this study (Bonavina, 2013) include the length of time and the patient population size. Downfalls include the small sample size who underwent post-operative esophageal pH monitoring and the strict patient selection criteria. The strict parameters under which MSA can be performed as outlined by this study, such as no worse than Los Angeles Class B esophagitis, indicate the lack of universal efficacy this procedure may have for GERD.

Further studies are needed to prove or disprove that theory. However, the success of the procedure for those who fit the parameters is not to be unnoticed. This highlights the fact that GERD is a spectrum and has many subjective and objective variables, of which more studies need to be performed to control for, in order to answer this research question.

### Comparison of Nissen Fundoplication and Magnetic Sphincter Augmentation

One of the first research projects to compare NF and MSA directly was a retrospective case-control study by Louie et. al (2014). They prospectively collected data on patients who underwent MSA from September 2012 to December 2013 at a single Swedish medical center and compared their results to patients they identified from a prospectively maintained benign esophageal surgical database who had undergone NF from January 2010 to July 2013. There were 34 patients who underwent MSA, and 24 completed six-month follow-up. Of the 98 NF database patients who qualified for comparison, 32 were selected based on MSA response group size, baseline demographics, and GERD characteristics. The groups were matched based on age, gender, BMI, symptom duration, hernia size, and esophagitis classification. The main differences between the two groups were MSA patients were older on average, and NF patients weighed more. Intraoperative times and adverse events were included in the study. Comparisons that showed statistical significance were made between the two groups on ability to belch and pH testing.

The mean operation time for MSA was 73 minutes, the mean operation time for NF was 118 minutes ($p = 0.001$), and no intraoperative deaths occurred in either group. Compared to themselves, both surgeries showed a significant decrease in heartburn, regurgitation, chronic cough, aspiration, chest pain, and ear, nose, and throat symptoms (throat clearing, hoarseness) at 6 months (Table 5), but there was no statistical difference between each other for any of those

parameters. GERD-HRQL scores improved from baseline, as well, but there was no statistical difference between the groups. The ability to belch showed a statistical significance in favor of MSA; 16 of the 24 patients were able to belch at six months, but no NF patients were able to ($p = 0.0001$). There were 18 of the 34 MSA patients who underwent pH testing at 6 months, and 22 of the 32 NF patients did. MSA and NF both normalized mean DeMeester scores, with MSA decreasing from 49.5 to 14.2 and NF from 59.0 to 5.1. The percentage of time with a $pH < 4$ was normalized in both groups, as well, with MSA decreasing from 14.8% to 4.6% and NF decreasing from 13.5% to 1.1%. There is a statistical difference between the two groups in favor of NF for both parameters, as NF improves both more drastically than MSA ($p = 0.0001$).

Table 5.

*Symptom resolution by MSA and NF*

| | Magnetic Sphincter Augmentation | | | | Laparoscopic Nissen Fundoplication | | | |
|---|---|---|---|---|---|---|---|---|
| | | Symptom Present Postoperatively? | | | | Symptom Present Postoperatively? | | |
| Symptoms | Preoperative | No (No.) | Yes (No.) | *p* Value[a] | Preoperative | No (No.) | Yes (No.) | *p*-Value[a] |
| Heartburn | No | 31 | 3 | 0.000 | No | 28 | 1 | 0.001 |
| | Yes | 31 | 2 | | Yes | 31 | 4 | |
| Regurgitation | No | 34 | 6 | 0.000 | No | 30 | 3 | 0.001 |
| | Yes | 28 | 0 | | Yes | 29 | 2 | |
| Cough | No | 31 | 27 | 0.000 | No | 31 | 22 | 0.001 |
| | Yes | 7 | 2 | | Yes | 10 | 1 | |
| Aspiration | No | 32 | 28 | 0.000 | No | 31 | 29 | 0.001 |
| | Yes | 6 | 0 | | Yes | 3 | 1 | |
| Chest pain | No | 32 | 25 | 0.000 | No | 32 | 26 | 0.001 |
| | Yes | 9 | 2 | | Yes | 6 | 0 | |
| ENT symptoms | No | 32 | 15 | 0.000 | No | 31 | 24 | 0.001 |
| | Yes | 19 | 1 | | Yes | 8 | 1 | |

[a] Related samples McNemar's change test.

ENT = ear, nose, and throat.

Limitations of this study include a significantly small sample size and short follow-up. This study is also retrospective, which could allow for selection bias. The authors report the patients in the NF group were carefully selected with that awareness in mind and that the patients would all have qualified for MSA, in attempts to mitigate that bias. Larger sample sizes, longer follow-up times, and perhaps a prospectively designed study would strengthen the evidence of this article. A benefit of this study was including the dietary protocols post-operatively for the

two surgeries. That feature might be viewed as a marker of efficacy to patients receiving the surgery, and it is an important piece of knowledge for readers to know when managing GERD patients. This study is applicable to this research question as it directly compared the two surgical techniques in question.

Sheu et. al. (2014) also reported a single institution, case-control study comparing patient-matched MSAs and NFs performed between 2012 and 2013. They identified 12 patients who underwent MSA at Massachusetts General Hospital during that time frame. They then identified 12 matching patients (based on age, gender, GERD symptoms, and hiatal hernia size) who underwent NF in the same time frame and performed a statistical analysis on the data collected regarding intraoperative time, length of hospitalization, resolution of GERD symptoms, dysphagia and the need for dilation, and operation side effects, including bloating, flatulence, and diarrhea. Results are as follows.

The average time to perform the operation was shorter for MSA compared to NF in this sample size (64 versus 90 minutes, $p < 0.001$). The length of hospitalizations were equivalent between the two groups, and there were no morbidities, mortalities, or re-admissions for either procedure. The average follow-up time for patients reporting subjective responses was 7 months. 75% of patients who underwent MSA and 83% who underwent NF reported resolution of their pre-operative GERD symptoms; there was no statistical difference calculated. The only statistically significant difference between MSA and NF in this study was post-operative dysphagia requiring a dilation. 50% (n=6) of MSA patients required an endoscopic dilation for severe dysphagia ($p=0.014$). 58% of NF patients did report some level of dysphagia post-operatively, but none required dilation. No patients in the MSA group reported persistent

bloating, flatulence, or diarrhea symptoms after surgery, and 33% of NF patients did, but there was not a statistical difference between the two groups.

The limitations of this study include a severely small sample size, which affects validity and applicability of all of the results. The study being retrospective and non-blinded, isolated to one hospital, and short-term also limits strength. A larger, randomized, longer-term study would strengthen evidence. Another limitation to this study includes the lack of use of a validated questionnaire, such as the GERD-HRQL. This can skew results as the way the questions are asked (which was not included in the study) can influence responses. No post-operative objective evaluations were included, either.

Reynolds et. al. (2016) performed a retrospective analysis of patients who underwent MSA or NF at a single facility between January 2010 and June 2013. The primary outcomes of the study were comparisons of hospital charges, complications, and outcomes of the procedures at one year. As surgical pricing is not applicable to this research question, information comparing prices were excluded from this literature review. There were 119 patients included in the study – 52 MSA and 67 NF patients. Between the two groups, there were more males in the MSA group, but outside of that there were no major differences in age, BMI, pre-operative GERD-HRQL score, hiatal hernia presence, laryngeal or pharyngeal reflux symptoms, Barrett's esophagus, or esophagitis classification.

Regarding 1-year outcomes, 48 of 52 MSA patients and 59 of 67 NF patients completed follow-up. No statistical difference was found between the two groups in GERD-HRQL scores. The mean score at one year was 4 for MSA and 5 for NF. Both groups had a significant decrease in PPI usage at one year. The study states that 85% of MSA and 92% of NF patients reported being completely off PPIs at the time of surveillance. There was no statistical difference between

the two groups. In the MSA group, 23% reported gas-bloat side effects 1 year after surgery, whereas 53% reported the symptom in the NF group ($p \leq 0.01$). The same statistical significance in favor of MSA was found for inability to belch (10 versus 36%, $p \leq 0.01$) and inability to vomit (4 versus 19%, $p \leq 0.01$). Patients were overall satisfied between the two groups with the surgery they had; 94% of MSA 85% of NF patients reported they would have the procedure again (no statistical difference between the two).

Limitations to this study again include a small sample size. Additionally, one of the authors disclosed serving as a consultant for Torax Medical, the company which invented MSA. The other six authors have nothing to disclose. Regardless, this study is still applicable to this research question as it directly compares the two procedures in question, reveals the efficacy of the two procedures, and shows statistical significance in some parameters between the two procedures..

An article by Warren et. al. (2015) conducted a multi-institutional retrospective cohort study at three high-volume surgical centers which brought in a larger pool of patients for data collection. The study identified 455 patients as having one of the procedures done during their set time frame. The cohorts were similar in terms of age, gender, and GERD-HRQL scores, but varied largely in BMI, dysphagia, DeMeester scores, Barrett's esophagus, and hiatal hernia. The authors reported outcomes at one year for all patients, but they also performed a propensity-matched analysis of the two surgeries, which will be summarized below. Propensity analysis further matched patients on esophagitis grading, Barrett's esophagus, hiatal hernia size, and BMI. The purpose of the study was to verify MSA's utility compared to NF in similarly-matched patients. Primary outcomes included GERD-HRQL scores, post-operative PPI usage, the ability to belch or vomit, and patient satisfaction.

The propensity-matched analysis compared 114 MSA patients to 114 NF patients. GERD-HRQL scores were low for both groups post-operatively, but there was no statistical difference between the two. MSA patients returned to using PPIs at higher percentages than NF patients (24 versus 12%, $p = 0.02$). MSA patients reported a higher ability to belch and vomit compared to NF patients (97 versus 66% and 88 versus 40%, respectively, $p < 0.001$). Patient satisfaction was high in both groups, but more MSA patients would undergo the surgery again (93 versus 83%, $p = 0.01$).

It is important to note that these results have been gathered from specialty centers, which may limit and skew the applicability of the results, as patient expectations and mentality of being at a specialty center may skew subjective responses and not be reproducible in general medical facilities. The fact that this is a retrospective analysis may also subject the results to inherent biases. Three of the authors also disclosed being consultants with Torax Medical, the company which invented the MSA device. This may have been unavoidable as this study took place over the time period when MSA was being trialed for FDA approval. Lastly, no objective measurements were used in the comparison. This study could be strengthened by either redesigning it in a prospective fashion, excluding brand consultants, or including objective measurements such as pH testing. Despite this, this article is applicable to the research question as it directly compared the two surgeries in question.

A meta-analysis by Chen et. al. (2017) also brought together larger pools of data comparing MSA and NF. They conducted a search of articles from 2005 to 2016 on PubMed, EMBASE, OVID, and Cochrane. Articles were included if they directly compared the two surgeries and reported on adverse events, complications, and PPI use. Risk ratio (RR), 95% CI, and p-values were included from the articles or were calculated by the authors if not done in the

original research. Four homogenous retrospective studies fit selection criteria, and post-surgery PPI use, complications, and adverse events of the surgeries were reported.

There were 624 patients included in the analysis; 299 in the MSA group and 325 in the NF group. The groups were similar in gender, age, and BMI. MSA had a shorter intraoperative time (RR=-18.80, 95% CI -24.57 - -13.04, p = 0.001) and length of stay (RR=-14.21, 95% CI -24.18 - -4.23, p = 0.005) compared to NF. There was no statistically significant difference in patients returning to PPIs for either surgery (RR = 1.21, 95% CI 0.89-1.65, p = 0.23). Three of the four articles this meta-analysis analyzed are included individually in this literature review, and individual reports of PPI usage are reported in their respective summaries. The authors defined surgical complications as post-operative dysphagia and dysphagia requiring a second surgery. Neither parameter showed a significant difference favoring one surgery over the other for avoiding either complication. There was a statistical difference in favor of MSA for a lower likelihood of gas or bloating post-operatively (RR=0.71, 95% CI 0.54-0.94, p = 0.02).

Even though there was only one statistically significant parameter derived, this study is beneficial to this literature review as it directly compared the two procedures using a large sample size. One limitation noted by the authors was that two of the four trials did not match hiatal hernia size. This may have affected the gas or bloating statistic, as the quality of hernia repair contributes to the tightness of the fundoplication in NF, which if too tight can cause gas and bloating symptoms. Additionally, all of the studies were retrospective, which has inherent biases. The authors report investigating for and avoiding publication bias through checking their data with funnel plots.

Another systematic review and meta-analysis conducted by Skubleny et. al. (2017) aims to also directly compare the efficacy of MSA and NF. The authors screened 197 titles and

abstracts from a variety of scholarly search engines, and three studies, two retrospective case controls and one prospective case control, met selection criteria. These non-randomized studies were then quality assessed with the validated Methodological Index for Non-Randomized Studies. Primary outcomes of interest included GERD-HRQL scores, DeMeester scores, intraoperative time, the ability to belch and vomit, PPI use, need for dilation, patient satisfaction, and presence of bloating and dysphagia. Statistical comparisons were able to be made between the two groups for ability to belch and vomit, PPI use, need for dilation,

The authors identified 688 patients. 273 underwent MSA, and 415 underwent NF. The mean follow-up time was between 7 and 16 months for MSA and 7 and 12 months for NF. There was a statistically significant superiority of MSA to NF in retaining a patient's ability to belch (95.2 versus 65.9%, $p < 0.00001$) and ability to vomit (93.5 versus 49.5%, $p < 0.00001$). There was no statistical significance between the two surgeries for gas-bloating symptoms, post-operative dysphagia, or PPI elimination. Six patients required an endoscopic dilation post-MSA, but none required it post-NF. The authors analyzed this parameter in other studies that did not fit selection criteria and state they have similar trends. GERD-HRQL scores improved drastically for both groups (20.5 to 3.0 for MSA and 19.7 to 3.2 for NF), but there was not a statistical difference between the groups. DeMeester scores followed a similar pattern with an improvement seen in both groups but no statistical significance between the two (49.5 to 14.2 for MSA and 49.0 to 5.1 for NF).

Limitations of this study, as highlighted by the authors, include a small number of studies utilized in compiling data. The authors highlight at the beginning that they are the first systemic analysis and systematic review comparing these two surgeries. Few studies in general have been performed directly comparing these surgeries. More need to be performed or inclusion criteria

should be expanded to include more studies to strengthen the evidence of this article. There were two studies that met inclusion criteria but were excluded due to the crossover of patients between collaborative studies, which ended up excluding 166 patients. The potential for larger sample size and more information was there but was not able to be utilized due to potentially repeated information. Due to the small sample size, results may be underpowered. More original studies should be performed to allow for a systematic review and meta-analysis with stronger evidence. Only conducting descriptive statistics may also be a limitation. Performing inferential statistics could have revealed more information. However, this article still highlights the efficacy of MSA compared to NF and is relevant to this research question as it directly compares the two surgeries in question.

## Discussion

The overarching theme presented in this cohort of research is that GERD is a highly variable disease due to its multitude of subjective and objective components, and there will likely never be a one-size-fits-all treatment option. The entire first theme is dedicated to the battery of tests performed to stratify the cause of a patient's GERD-like symptoms. These thorough and validated tests serve to accurately sift through a complex interplay of symptoms and mucosal changes to determine who would benefit best from surgery. However, patient habitus, diet, and lifestyle are significant components of GERD as well and have not and potentially cannot be accounted for in a GERD work-up.

Among the surgical treatment options, it is apparent why Nissen fundoplication has served as the gold standard. It has stood the test of time as a durable treatment option, as highlighted by Anvari and Lafullarde's articles. It has also improved with time and surgical advances, as demonstrated by DeMeester's historic 1986 article, which has resulted in an

improved side effect profile. With these advancements, it has also been shown in Prassas's 2017 article that similar levels of efficacy can be achieved when this procedure is performed by a general surgeon in a low-volume community hospital and not just a foregut specialist.

Magnetic sphincter augmentation seems to also be showing promise as a durable treatment option. Ganz et. al. (2016) report efficacy out to five years in their patient population. Bell et. al. (2019) report efficacy of the device as well with objective reduction of esophageal acid exposure and subjective reduction of symptoms, however, only out to one year. It will take time to reveal longer-term efficacy, but shorter-term studies available at this time reveal positive results. Another fault of its infancy is the small sample size featured in all of the articles available at the time of this scholarly project. Small sample sizes easily skew data by either under or overpowering results, so while evidence is promising at this point, that is a fact to remain cognizant of.

Compared head to head, MSA and NF both consistently improve GERD-HRQL scores, but no data showed clear superiority of one surgery over the other in any consistent pattern. The articles by Sheu (2014) and Louie (2015) reveal that while both reduce DeMeester scores and esophageal acid exposure time to below pathologic levels, NF reduces that time significantly more. This could be due to NF producing a tighter reinforcement of the LES than MSA. The magnetics in MSA are calibrated to open and close with pressures equivalent to what a normal esophagus produces when moving a bolus of food and pressures exerted by a normally-functioning stomach in a patient of normal BMI. NF is "calibrated" using a bougie to dilate the esophagus. The size of the bougie is generally based on surgeon preference. The fact that MSA eliminates pathologic reflux indicates that the procedure is adequate, but NF may be a superior option for complete acid reduction.

The articles by Chen (2017), Reynolds (2016), Skubleny (2017), and Warren (2015) all reveal that MSA produces a lower side effect profile of gas-bloat symptoms, inability to belch, and inability to vomit. This again could be due to NF producing a tighter reinforcement of the LES than MSA, but it could also be due to the design of the two surgeries, as MSA preserves gastric anatomy, but NF does not. However, in one study (Ganz, 2016), three patients who underwent MSA experienced dysphagia that resolved with an NF. That trend was not seen anywhere else. The data collected by Warren et. al. (2015) showed that patients who underwent MSA returned to PPI therapies at higher rates than patients who underwent NF, but the data collected by Chen (2017) and Skubleny (2017) did not.

While some clear and objective takeaways may be able to be made regarding the advantages of one surgery over the other, it is crucial to note that many of these articles contain small sample sizes, short follow-up times, and potential conflicts of interest in favor of MSA. Small sample sizes can under or overpower results and may give results that cannot be reproduced on a larger scale. Short follow-up times may miss potential complications of MSA that are not experienced until five, ten, or more years down the road. Torax Medical, Inc. sponsored the study conducted by Bell et. al (2019), and the articles by Reynolds (2016) and Warren (2015) had one or more authors who disclosed they were Torax consultants. This creates bias and potential conflict of interest in some of the articles, which may be unavoidable at the stage in MSA's advent. The other articles in this scholarly project which do not have bias or conflict of interest by corporate sponsorship reveal similar results, but it is important readers do not completely dismiss the presence of the bias.

In summary, GERD is a multifactorial and highly individual disease process. While both procedures are effective in controlling reflux with the data reviewed, MSA does not have as

robust evidence in its support when compared directly to NF at this time. As always, individual diagnostics, symptoms, and patient goals should be taken into careful consideration when selecting which surgical option to utilize. The existing data is promising in MSA's utility and efficacy. I look forward to watching this procedure develop and adapt as our knowledge of this dynamic disease progresses.

## Clinical Application

With the information provided in this scholarly project, readers can understand the utility and efficacy of the newest anti-reflux surgery available. This will allow physician assistants in primary care and general surgery to continue to provide the best education on GERD management, including the pros and cons of PPIs versus surgical therapy, the steps needed to explore surgical therapies, the potential surgical options, and the side effects and possible outcomes of these two procedures. It will also help primary care providers to make informed surgery referrals and provide the best pre-operative and post-operative care.

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