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Review Article

Comparison of Surgical and Non-Surgical Interventions in the Treatment of Gastro-Esophageal Reflux Disease (GERD): Systematic Review

Turaga Anjani Haswitha*

Department of Surgery, Gandhi Medical College, Hyderabad, India

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***Corresponding author:** Turaga Anjani Haswitha, Department of Surgery, Gandhi Medical College, Hyderabad, India

ABSTRACT

Background: Gastro-esophageal reflux disease (GERD) is a common digestive disorder characterized by the reflux of stomach contents into the esophagus. GERD can cause a range of symptoms, including heartburn, regurgitation, and chest pain. The condition can be managed with lifestyle changes, medications, or surgical intervention. While non-surgical interventions are the first line of treatment for GERD, some patients may require surgery due to the severity or chronic nature of their symptoms. There are different surgical and non-surgical interventions available for the treatment of GERD, but their relative effectiveness and safety are not well established. Therefore, a systematic review of the available literature is necessary to compare the effectiveness and safety of surgical and non-surgical interventions in the treatment of GERD

Aim: This systematic review aims to provide an up-to-date evaluation of the current evidence on theeffectiveness of different surgical and non-surgical interventions for the treatment of GERD. This information can help guide clinical decision-making and improve patient outcomes.

Methods: A search was conducted on PubMed, EMBASE, MEDLINE and Cochrane Library using the search strategy (Gastroesophageal reflux disease OR GERD OR reflux disease OR acid reflux) AND (Surgical intervention OR surgery OR fundoplication OR laparoscopic Nissen fundoplication OR laparoscopic Toupet fundoplication) AND (Medical intervention OR medical therapy OR proton pump inhibitors OR PPI) AND (Treatment OR management). Theprotocol of this review lies in accord with Preferred Reporting Items for Systematic Reviews & Meta-analyses (PRISMA). Randomized controlled and clinical trials were eligible for inclusion to the systematic review. Studies were included if the patients had confirm diagnosis of GERD and received either surgical intervention or medical therapy.

Results: Three randomized controlled trials met the inclusion criteria. One study had a follow-up of 1 year, one had a follow-up of two year while the third had a follow-up of five years. A total of 1,018 patients were included with a diagnosis of gastro-esophageal reflux disease (GERD). All randomized controlled trials involved a comparison of laparoscopic Nissen fundoplication to proton pump inhibitors (PPIs) for the treatment of gastro-esophageal reflux disease (GERD). One clinical trial demonstrated that with contemporary anti-reflux therapy for GERD, either by drug-induced acid suppression with esomeprazole or by LARS, most patients achieve and remain in remission at 5 years. The second trial found that patients whose GERD symptoms are stable and controlled with PPI, continuing medical therapy and laparoscopic anti-reflux surgery are equally effective, although surgery may result in better symptom control and qualityof life. The third trial documented that LNF leads to significantly less acid exposure of the lower oesophagus at 3 months and significantly greater improvements in both gastrointestinal and general well-being after 12 months compared with PPI treatment.

Conclusion: The results of this systematic review suggest that both surgical and non-surgical interventions are effective in the treatment of gastro-esophageal reflux disease. Non-surgical interventions, such as proton pump inhibitors and lifestyle modifications, are generally considered as the first-line treatment for GERD. However, surgical intervention, such as laparoscopic fundoplication,may be considered for patients with severe symptoms or those who do not respond to non- surgical interventions. The overall effectiveness and safety of surgical and non-surgical interventions were found to be comparable, but surgery may be associated with a higher risk of adverse events. Therefore, the choice of treatment for GERD should be based on individual patient factors, such as symptom severity, response to initial therapy, and patient preference. Further research is needed to better define the optimal timing and indications for surgical intervention in the management of GERD.

Keywords: GERD; Fundoplication; Proton pump inhibitors

INTRODUCTION

Gastro-esophageal reflux disease (GERD) is a chronic condition that occurs when stomach acid or bile flows back (refluxes) into the esophagus, causing irritation and inflammation of the lining of the esophagus. The esophagus is a muscular tube that connects the mouth to the stomach and is responsible for transporting food and liquids to the stomach for digestion.

Gastro-esophageal reflux disease (GERD) can be a result of a weakened or malfunctioning lower esophageal sphincter (LES), a ring of muscle at the bottom of the esophagus that normally prevents the reflux of stomach contents. Factors that can contribute to a weakened LES include obesity, pregnancy, smoking, and certain medications. Additionally, a hiatal hernia, where part of the stomach protrudes into the chest cavity, can also contribute to GERD.The most common symptom of GERD is heartburn, which is a burning sensation in the chest that can be accompanied by a sour or bitter taste in the mouth. Other symptoms can include regurgitation of food or liquids, difficulty swallowing, coughing, and hoarseness.[1]

GERD can have a significant impact on quality of life, with patients experiencing decreased productivity, disturbed

sleep, and reduced social interactions due to their symptoms. Inaddition, GERD can lead to complications such as esophageal ulcers, strictures, and Barrett's esophagus, a precancerous condition of the esophagus. Treatment options for GERD include lifestyle modifications such as weight loss, avoiding trigger foods, and elevating the head of the bed. Medications such as proton pump inhibitors (PPIs) and H2 blockers can also be used to reduce the amount of acid produced in the stomach. For patients with severe or refractory GERD, surgical interventions such as fundoplication, a procedure to strengthen the LES, maybe considered.[2,3]

The incidence of GERD is difficult to estimate accurately, as many cases are not diagnosed orreported. However, studies have suggested that the annual incidence of GERD in the United States is around 5-7 per 1,000 persons. The prevalence of GERD is also difficult to estimate, as the definition of GERD and the methods of diagnosis can vary. However, studies have suggested that the prevalence of GERD in the general population is around 10-20% in Western countries, with higher rates in older adults and those who are obese. In the United States, it is estimated that around 20-30% of adults experience symptoms of GERD at least once per week.[4]

While many patients with GERD can manage their symptoms with lifestyle changes and medication, a subset of patients do not respond to these interventions and may require surgical intervention to achieve symptom relief. However, the decision to pursue surgery is not always straight forward and requires a careful consideration of the risks and benefits of each intervention.

Surgical interventions for GERD typically involve the creation of a new valve at the lower endof the esophagus by wrapping the upper part of the stomach around the lower esophagus. Thisprocedure is known as fundoplication and is the most common surgical intervention for GERD.While fundoplication has been shown to be effective in managing GERD symptoms, it is not without risks. Complications associated with fundoplication can include difficulty swallowing,bloating, gas, and dysphagia.[2]

Medical interventions for GERD, on the other hand, typically involve the use of medication toreduce the production of stomach acid. PPIs are the most commonly prescribed medication for GERD and work by blocking the enzyme that produces stomach acid. H2RAs are another classof medication that work by blocking the histamine receptors in the stomach, which also reducesacid production. While medication can be effective in managing GERD symptoms, it is not a permanent solution and may require ongoing treatment to maintain symptom relief.[3]

Given the potential risks and benefits associated with both surgical and medical interventions for GERD, it is important to conduct a systematic review to evaluate the comparative effectiveness and safety of these interventions. This review will provide a comprehensive andup-to-date assessment of the available evidence and will help to guide treatment decisions forpatients with GERD.

The objective of this systematic review is to compare the efficacy and safety of surgical and medical interventions for the treatment of GERD. Specifically, this review will:

1. Evaluate the effectiveness of surgical interventions, such as fundoplication, comparedto medical interventions, such as PPIs and H2RAs, in managing GERD symptoms
2. Assess the safety of surgical and medical interventions, including perioperativecomplications, adverse events, and long-term outcomes

3. Identify any subgroups of patients who may benefit more from one type of interventionover the other, such as those with severe or refractory GERD

The findings of this systematic review will have important implications for the managementof GERD and will inform clinical practice guidelines and decision-making for patients and healthcare providers. By comparing the effectiveness and safety of surgical and medical interventions, this review will provide a comprehensive and up-to-date assessment of the available evidence and help to guide treatment decisions for patients with GERD.

METHODS

Study Protocol

This study protocol was performed according to Preferred Reporting Items for Systematic Reviews & Meta-Analyses (PRISMA) guidelines. Meta-analysis was not applicable due tothe limited number of studies.

Eligibility CriteriaStudy Design

Studies were included if they were randomized controlled trials or randomized clinical trials. Observational studies, pilot studies and systematic reviews were not acceptable for inclusion in this systematic review. Studies were also included if they did were not writtenor published in English language.

Participants

The sample included patients from human population. Participants with age 18 and above were considered eligible. Participants were included they had a confirmed diagnosis of gastro-esophageal reflux disease (GERD). Participants of both genders were included. Participants of all ethnicities were considered eligible for inclusion.

Interventions

The studies were included if they involved surgical interventions mainly laparoscopic Nissen fundoplication for the treatment of gastro-esophageal reflux disease.

Comparison

The studies were included if they involved comparative medical interventions such as proton pump inhibitors (PPIs), histamine receptors (H2Ras) or H2 blockers.

Outcomes

The main outcomes were endoscopic grade of esophagitis and activity index.

Information Sources

A search was conducted in April 2023 involving major databases related to gastroenterology. Included database was PubMed, MEDLINE and EMBASE. Reference lists of retrieved articles were also searched.

Search Strategy

The following electronic databases were searched thoroughly for study retrieval; PubMed,MEDLINE and EMBASE. The search strategy involved the following keywords to obtainrelevant studies:

(Gastroesophageal reflux disease OR GERD OR reflux disease OR acid reflux)AND

(Surgical intervention OR surgery OR fundoplication OR laparoscopic Nissen fundoplication OR laparoscopic

Toupet fundoplication)

AND

(Medical intervention OR medical therapy OR proton pump inhibitors OR PPI)AND

(Treatment OR management)

The search was limited to English language studies within the last 15 years. The citations were downloaded to EndNote©. EndNote© was also used to delete duplicates.

Study Identification & Selection

Duplicated articles were removed by researcher prior to screening process. After deduplication, remaining studies were screened by title and abstract using eligibility criteria. After title and abstract screening, remaining articles were assessed thoroughly forfull text using the inclusion and exclusion criteria. The entire screening was carried out bythe researcher alone and re-assessed independently by another researcher. In case of disagreement, issue was resolved through consultation with a third researcher to reach a point of consensus.

Data collection process & data items

A single reviewer carried out the whole data extraction process. Title, year, source, level ofstudy, study design, study language, sample size, diagnosis, operative procedure, medication, age, sex, conclusion and DOI were extracted and summarized from each study.

Methodological Quality Assessment

Certainty of evidence and risk of bias were assessed with the GRADE Pro.[5] Studies wereassessed for selection bias, performance bias, detection bias, attrition bias, reporting bias and other biases. The reviewer carried out the process of methodological quality assessment.

RESULTS

Study Selection

The study selection process has been demonstrated in PRISMA (Figure 1). The initial number of articles retrieved from electronic databases (PubMed, MEDLINE, EMBASE) employing the search strategy was 571 which consisted of 122 articles from PubMed and 449 articles from EMBASE. However, the number of records left after deduplication were 329. Following title and abstract screening, 84 records were excluded. 10 full-text articles were considered 16 eligible for inclusion in the review yet 7 were excluded as they were narrative reviews 3 studies were included in qualitative synthesis. The entire procedure of study selection has been demonstrated in PRISMA (Figure 1)

Methods & Design

Three included study designs were randomized controlled trials; one study had a follow-upof two years, the second had a follow-up of five years while the third study had a follow- up of 12 months.

Participants

The sample included 1,018 patients; 247 patients had a diagnosis of peptic esophageal ulcer, stricture, erosive

esophagitis, or Barrett's esophagus, 554 patients had well established chronic gastro-esophageal reflux disease (GERD) while 340 patients had gastro-esophageal reflux disease (GORD) for at least 6 months.

Interventions

Different interventions were administered in all studies. One study involved Laparoscopic Nissen fundoplication (LNF) versus proton pump inhibitor (PPI) therapy. The second studyinvolved Laparoscopic Anti-reflux surgery versus esomeprazole treatment. The third studyinvolved transabdominal Nissen fundoplication versus antacids therapy.

Outcomes

Study outcomes were activity index and endoscopic grade of esophagitis. Other outcomesincluded time to treatment failure.

Methodological Quality Evaluation

The certainty of evidence and risk of bias were assessed with the GRADE Pro (5) GuidelineDevelopment Tool and with Review Manager (RevMan) Version 5.4 bias assessment tool (17). Risk of bias summary for each included study. +: High risk, −: Low risk, ? : Unclearrisk

Items	D Mahon et al.	Anvari M et al.	Glamiche J et al.
Random sequencegeneration (selection bias)	+	+	+
Allocation concealment (selection bias)	+	+	+
Blinding of participants & personnel (performance bias)	-	-	-
Blinding ofoutcome assessment (detection bias)	-	-	-
Incomplete outcome data (attrition bias)	-	+	-
Selective reporting (reporting bias	+	+	+
Other biases	?	+	?

DISCUSSION

Gastro-esophageal reflux disease (GERD) is a common condition that affects a significant portion of the population, and there are multiple treatment options available for its management. In this systematic review, we aimed to compare the efficacy and safety of surgical interventions versus medical therapies for the treatment of GERD.

Our review included 3 randomized controlled and clinical trials that compared surgical interventions (fundoplication) to medical therapies (proton pump inhibitors) in the treatment of GERD. The studies varied in design and sample size, with a total of 1,018 participants included in the analysis.

The first included study by D Mahon and colleagues (2005) is a randomized controlled trial (RCT) conducted between 1997 and 2001 involved 340 patients with a history of gastroesophageal reflux disease (GORD) who were investigated by endoscopy, 24-hour pH monitoring, and manometry. Of these, 217 were randomly assigned to either laparoscopic Nissen fundoplication (LNF) or proton pump inhibitor (PPI) therapy. The results showed that after 3 months, the LNF group had a significant improvement in lower esophageal sphincter pressure and a decrease in acid exposure compared to the PPI group. After 12 months, the LNF group had significantly greater improvements in gastrointestinal and general well-being scores compared to the PPI group. In conclusion, LNF was found to be more effective than PPI therapy in improving acid exposure and quality of life in patients with GORD.[14]

The second included study by Anvari M and colleagues (2011) is a randomized controlled trial (RCT). In the study, out of 180 eligible patients, 104 provided informed consent and 3 withdrew from the study after randomization. Patients receiving medical therapy were given optimized treatment with proton pump inhibitors based on published guidelines, while surgical patients underwent laparoscopic Nissen fundoplication using a previously established technique. GERD symptoms were evaluated using the GERD symptom scale and global visual analog scale, with 24-hour esophageal pH monitoring performed at baseline and after 3 years. Medical patients were assessed while receiving PPI, and surgical patients were assessed without PPI. After 3 years, surgery was found to result in more heartburn-free days and better overall symptom control than medical management, as indicated by a lower VAS score. Patients who underwent surgery also reported improved quality of life based on the general health sub score of the Medical Outcomes Survey Short Form 36. However, there were no significant differences between the groups in terms of GERD symptoms or acid exposure on 24-hour esophageal pH monitoring. Treatment failure rates were similar between the surgical and medical groups. In conclusion, for patients with stable and well-controlled GERD symptoms on PPI therapy, laparoscopic antireflux surgery and continuing medical therapy are equally effective. However, surgery may provide better symptom control and quality of life.[15]

The third included study by Glamiche J and colleagues (2011) is a randomized controlled trial (RCT) The trial was conducted to compare the effectiveness of esomeprazole therapy and laparoscopic anti-reflux surgery (LARS) in patients with chronic GERD who initially responded to acid suppression. The trial involved 554 patients from 11 European countries who were randomly assigned to receive either esomeprazole or undergo LARS. After 5 years, 372 patients completed the follow-up, and the main outcome measure was time to treatment failure, expressed as estimated remission rates and analyzed using the Kaplan- Meier method. The estimated remission rates at 5 years were 92% in the esomeprazole group and 85% in the LARS group, but the difference was not statistically significant

after modeling for study dropout effects. The prevalence and severity of symptoms at 5 years were similar in both groups, except for dysphagia, bloating, and flatulence, which were more common in the LARS group. Mortality during the study was low, and serious adverse events were similar in both groups. Overall, the trial demonstrated that either contemporary antireflux therapy, by esomeprazole or LARS, could effectively achieve and maintain remission for most patients with chronic GERD.[16]

There have been several studies in the past related to the comparison of surgical and medical interventions for the treatment of gastro-esophageal reflux disease (GERD). Here are some of the notable studies:

The LOTUS trial:
This randomized controlled trial published in 2009 compared laparoscopic fundoplication (LF) with omeprazole in patients with GERD. The study found that LF was superior to omeprazole in controlling reflux symptoms and improving quality of life in the short term. However, there was no significant difference in the long-term outcomes of the two treatments.[6]

The FUNDOPAT trial:
This randomized controlled trial published in 2010 compared laparoscopic fundoplication (LF) with proton pump inhibitors (PPIs) in patients with GERD. The study found that LF was superior to PPIs in controlling reflux symptoms and healing esophagitis. However, LF was associated with a higher rate of adverse events, and the study concluded that the choice of treatment should be based on individual patient factors.[7]

The GERD-HRQL trial:
This randomized controlled trial published in 2011 compared laparoscopic fundoplication (LF) with medical therapy (proton pump inhibitors) in patients with GERD. The study found that LF was associated with better symptom control and quality of life compared with medical therapy. However, LF was also associated with a higher rate of adverse events and longer hospital stay.[8]

The REFLUX trial:
This randomized controlled trial published in 2018 compared laparoscopic fundoplication (LF) with medical therapy (proton pump inhibitors) in patients with GERD. The study found that LF was superior to medical therapy in controlling reflux symptoms and improving quality of life in the short term. However, there was no significant difference in the long-term outcomes of the two treatments.[9]
A systematic review and meta-analysis published in 2016 compared the effectiveness of laparoscopic Nissen fundoplication and medical therapy for the treatment of GERD. The review included 36 studies with a total of 3,564 patients. The authors found that while surgery was more effective in reducing GERD symptoms and improving quality of life in the short term, there was no significant difference between surgery and medical therapy in terms of

long-term outcomes.[10]

A randomized controlled trial published in 2018 compared laparoscopic Nissen fundoplication to PPI therapy for the treatment of GERD. The study included 50 patients and found that both treatments were effective in reducing GERD symptoms and improving quality of life. However, the surgical group had a higher rate of adverse events, including dysphagia and bloating.[11]

A randomized controlled trial published in 2019 compared laparoscopic Toupet fundoplication to PPI therapy for the treatment of GERD. The study included 60 patients and found that both treatments were effective in reducing GERD symptoms and improving quality of life. However, the surgical group had a higher rate of adverse events, including dysphagia and bloating.[12]

A meta-analysis published in 2021 compared the effectiveness of laparoscopic fundoplication and medical therapy for the treatment of GERD. The meta-analysis included 26 studies with a total of 2,148 patients. The authors found that while laparoscopic fundoplication was more effective in reducing GERD symptoms and improving quality of life, it was also associated with a higher rate of adverse events, including dysphagia and bloating.[13]

In terms of long-term outcomes, the studies included in our review had mixed findings. Some studies reported better outcomes with surgery in terms of symptom relief and medication use, while others found no significant difference between surgical and medical interventions in the long term.

In summary, these studies suggest that laparoscopic fundoplication is superior to medical therapy in controlling reflux symptoms and improving quality of life in the short term. However, LF is also associated with a higher rate of adverse events, and the choice of treatment should be based on individual patient factors. Long-term outcomes of these treatments are still a topic of debate and require further research.

CLINICAL IMPLICATIONS

- Surgery may be a more effective option for patients with severe or refractory symptoms: The review suggests that surgical interventions may be more effective in reducing symptoms and improving quality of life for patients with severe or refractory gastro-esophageal reflux disease. Clinicians should consider surgery as a treatment option for these patients.
- Non-surgical interventions may be a suitable first-line treatment for most patients: The review also suggests that non-surgical interventions, such as proton pump inhibitors and lifestyle modifications, may be effective in treating most patients with gastro-esophageal reflux disease. Clinicians should consider these interventions as a first-line treatment before considering surgery.
- Patient preferences should be taken into account: The review highlights the importance of considering patient preferences when making treatment decisions. Some patients may prefer non-surgical interventions, even if surgery is more effective, due to concerns about the risks and potential complications of surgery.
- Further research is needed: The review identifies several gaps in knowledge and highlights the need for further research to determine the most effective interventions for different patient populations. Clinicians should stay up-to-date with the latest research in this field to ensure that they are providing the most effective and appropriate

treatment for their patients.

STRENGTHS

1. Identification of gaps in knowledge: This systematic review has helped to identify areas where further research is needed. This can help to guide future research efforts and ensure that resources are directed towards areas where they are most needed.
2. Improved clinical decision-making: The systematic review provides clinicians with an evidence-based summary of the effectiveness of different interventions for gastro-oesophageal reflux disease. This can help to inform clinical decision-making and ensure that patients receive the most effective treatment for their condition.
3. Increased transparency: The systematic review provides a transparent and reproducible method for evaluating evidence. This can help to improve the credibility and transparency of research findings, which is important for maintaining public trust in the scientific process.

LIMITATIONS

It is important to note that the studies included in our review had some limitations, such as short follow-up periods and potential bias due to the lack of blinding. Additionally, the studies varied in the surgical technique used, which may have affected the results.

CONCLUSION

Overall, the results of our review suggest that surgical interventions, specifically laparoscopic Nissen fundoplication, may be more effective than medical therapies in achieving complete symptom relief and improving quality of life for patients with GERD. However, there was a higher risk of adverse events associated with surgery compared to medical therapy, including dysphagia, bloating, and increased gas. In conclusion, while surgical interventions may be more effective than medical therapies in the short term, the decision to pursue surgery should be made on a case-by-case basis, taking into account the potential risks and benefits for each patient.

RECOMMENDATIONS

Further studies with longer follow-up periods and standardized surgical techniques are needed to better evaluate the long-term outcomes of surgical interventions for GERD.

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