

Original Article

Fundoplication in Pediatric Achalasia Patients Undergoing Heller's Myotomy: A Systematic Review

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Abstract:

Background: Achalasia is a rare motility disorder, with the incidence being the lowest among children. The disease is caused by the inability of the LOS to relax and the absence of normal peristalsis of esophagus. Heller's myotomy has been known to be the gold standard management of achalasia, however, reports on postoperative GERD were established in the past. To control the reflux symptoms, fundoplication has been used as an addition to Heller's myotomy. Unfortunately, there has been an inconclusive finding from available studies regarding the need for performing fundoplication. Hence, we aim to determine whether or not the addition of fundoplication to Heller myotomy in achalasia children resulted in better postoperative outcomes and fewer complications of GERD.

Methods: A literature search was carried out in four databases: Medline, EMBASE, Pubmed, and Cochrane Library. The search was limited to publications from 2006 to 2019, English studies, and achalasia patients age 0-18 years old that underwent Heller's myotomy. The exclusion of studies from the primary screening according to title and abstracts and secondary screening on the full text were done according to a priori protocol. Duplicate studies were also eliminated by using reference management software and manually.

Results: A total of 446 studies were retrieved from the search. Preliminary screening based on the eligibility criteria resulted in 21 articles to be included in this review. A total of 410 patients were included in this study, in which 80 underwent HM alone and 330 experienced fundoplication as an adjunct to HM (HMF). There was a higher proportion of asymptomatic patients in the HM group (56.3%) compared to HMF (48.8%). Both groups had a similar rate of complications (HMF 12.1%, HM 10.0%). However, in terms of postoperative GERD, slightly better results were seen among HMF patients (9.7%) than HM (15%).

Conclusion: Fundoplication did not result in better resolution of symptoms, as seen from its percentage of asymptomatic patients. Improvements in postoperative GERD were seen in HMF patients, however, it was deemed as insignificant. The findings suggest that there was a limited benefit in using fundoplication.

Keywords: achalasia, children, fundoplication, GERD, Heller's myotomy

Introduction

Achalasia is a rare motility disorder of the esophagus, with a reported incidence of 0.11 for every 100000 children.¹ Achalasia is the rarest among children younger than 5 years old. This is supported by the fact that for every 100,000 children younger than the age of 16, on average 0.11 to 0.18 develop achalasia every year.^{2,3} In fact, only 5% of patients with achalasia report developing symptoms before they reach the age of 15.¹ Patients with achalasia experience difficulty in swallowing, as there is partial or total inability of the lower esophageal sphincter (LOS) muscle to relax, as well as the absence of normally coordinated esophageal peristalsis.⁴ This condition hinders the normal downward movement of the food bolus from the esophagus to the stomach, leading to various symptoms such as dysphagia, heartburn, chest pain, regurgitation, and weight loss. As a result, the long-term impact of achalasia includes significant impairment in the quality of life of those affected. A possible etiological explanation for achalasia is that there is a degeneration of the myenteric plexus and vagal nerve fibers of the LOS, which might occur due to autoimmunity or viral infection. However, despite this proposed mechanism, the etiology remains unclear.⁵

While it is known that Heller's myotomy (HM) has been the gold standard for decades in treating achalasia, there are cases in the past that have proceeded to complications.⁶ The adverse effects include esophageal perforations and gastroesophageal reflux, with the latter being the most common out of the two. This is due to the widening of the esophageal passageway from the HM, which allows fluid or solids to go downwards and hence upwards as well. Handling the reflux is necessary as it can lead to erosive esophagitis, Barret's esophagus, and even adenocarcinoma of the esophagus.⁷ In order to tackle this problem, concurrent anti-reflux procedures have been considered along with HM, and the method of choice is fundoplication in most cases.

Unfortunately, it is still debatable whether or not HM in conjunction with fundoplication should always be done, considering that there are pharmacological anti-reflux treatments that could be given to the patients. There is a possibility that fundoplication exacerbates the obstruction, due to it being done too tightly. In this case, post-operative dysphagia could occur.⁸ Despite the probability of it causing adverse effects, the use of fundoplication has been known to provide the best long-term reduction of GERD.⁹

The need to perform fundoplication in order to control GERD on pediatric achalasia patients who received HM is still inconclusive. Enough evidence on the efficacy and safety of fundoplication should be gathered to support its use, and to reduce doubts regarding its benefit. Therefore, this study aims to review whether the addition of

fundoplication in Heller’s myotomy patients leads to better improvement in swallowing without the post-operative complications of GERD.

Methods

The systematic review was performed under the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Search Strategy and Study Selection

Four electronic databases have been used for this systematic review as a source of information, which includes Medline (Ovid), EMBASE (Ovid), Pubmed, and Cochrane Library. The keywords used to do the search were achalasia, Heller’s myotomy, and children (based on PICO keywords presented in **Table 1**). The search strategy was created by the author and assessed by a librarian who is an expert in the field of literature searching. The most recent search was done on 7 November 2019, and results of each databases were attached in Appendix 2. Limits were applied to the searches in EMBASE only, so that only published articles as well and articles in press that were included to the search results.

Studies from the electronic database searching were exported into MEDLINE format, which resulted in the complete references within an excel sheet. The first screening of the studies was done based on the title and abstracts, according to the PICO components (**Table 1**). The full-text articles were obtained for studies with no abstract in the excel sheet. Another screening was then done through assessing the full-text articles using the inclusion and exclusion criteria as the filter (**Table 2**).

Table 1. PICO keywords

Patients/Population:	Pediatric achalasia patients receiving Heller’s myotomy
Intervention/Exposure:	Fundoplication
Comparator:	Without fundoplication
Outcome(s):	Reversal of achalasia symptoms (able to swallow) without the postoperative complications of GERD

Table 2. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Pediatric achalasia patients 18 years old or younger who received Heller’s myotomy	Patients older than 18 years old who did not have achalasia or not treated with Heller’s myotomy

Papers with either Heller's myotomy with fundoplication or Heller's myotomy without fundoplication.	Patients solely treated with other surgical interventions for achalasia
Papers with both Heller's myotomy with fundoplication and Heller's myotomy without fundoplication.	Studies without information on the symptoms before and after the surgery
Resolution of achalasia symptoms (able to swallow) without the postoperative complications of GERD	Non-English studies
English studies	Studies published before 2006
Studies published from 2006-2019	Animal/ non-human studies
Human studies	Systematic review and meta-analysis
Cohort or cross-sectional studies	Duplicate publications

Data Extraction

Studies from the four databases that have been screened and fulfil the eligibility criteria were exported to its RIS format and then be imported to EndNote X9. which is a reference management software. Duplicate studies will be eliminated both manually and using the "Find Duplicates" option in the software. After all of the duplicate studies has been eliminated, the articles were independently extracted by the reviewers to obtain certain data. The extraction was done through using Microsoft Excel version 16.31.

Risk of Bias and Quality Assessments

The assessments of the risk of bias and the quality of each paper were done by utilizing the Risk of Bias in Non-randomized Studies- of Interventions (ROBINS-I) tool. The first stage of ROBINS-I is the protocol stage, which contains the PICO component of this systematic review. The next stage focused more on each study being assessed, and it requires the reviewer to analyze the design and PICO of the study. The measurement of study bias was classified as before, at the time, and after the intervention. Responses to each component were either "Yes", "Probably Yes", "No", "Probably No", and "No Information".

Results

The search results from Medline (Ovid), EMBASE (Ovid), Pubmed, and Cochrane resulted in a total of 446 studies. The studies were then screened based on their title and abstract, which then proceeded to full-text screening. The final number of studies that are eligible to be included in the qualitative synthesis is 21. The reasons for

exclusion were provided in detail in the **Figure 1** below and is mainly due to the participants of the studies being older than 18 years old (n= 154).

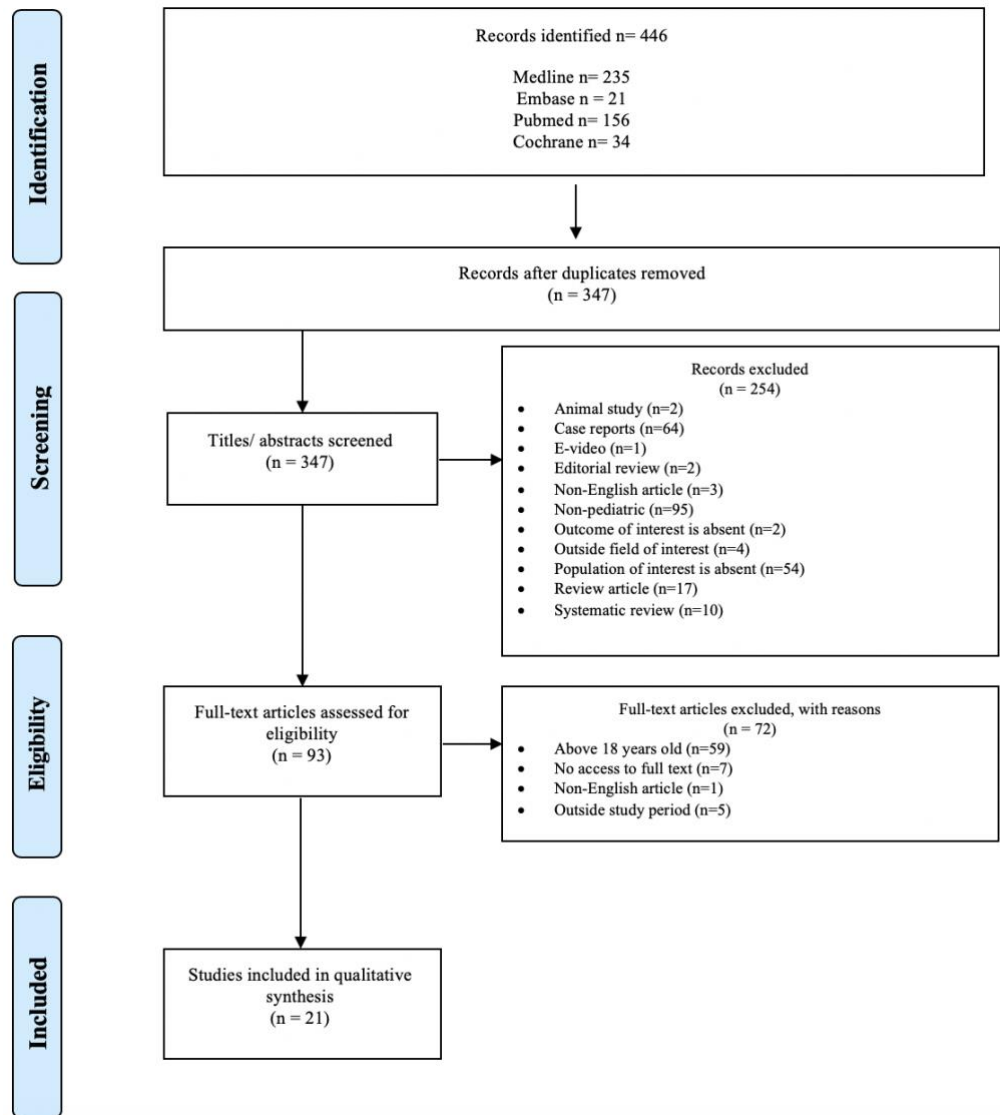


Figure 1. PRISMA flowchart

The study characteristics of all the studies that were included in the analysis were displayed in **Table 3**. The 21 papers consisted of 4 cohort studies (3 retrospective, 1 prospective), 6 cross-sectional studies, and 11 case series. The year of publication ranged from 2007 to 2019, and the span of the study period is from 1990 until 2017. A total of 410 patients were recruited, in which 80 patients underwent HM alone, and 330 underwent HM along with fundoplication. The participants of the included literatures consisted of 260 males and 210 females. However, the data of 60 patients contains those that did not take HM at all, as the studies have failed to mention the gender of secondary HM participants. Furthermore, the gender data also includes

those that were excluded in the study. An average of patients age was not able to be calculated since a subset of the studies provided only the age of diagnosis and not at surgery.

Risk of Bias

The risk of bias assessment using the ROBINS-I tool concluded that the 21 articles had either a low or a moderate risk of bias for all domains. Therefore, an overall judgement of moderate risk was given to every included study, based on the criteria stated in the ROBINS-I guideline.

Primary Outcomes

Among patients of the HMF group, there were 12 (3.6%) relapse cases, and partial improvements of the preoperative achalasia symptoms were seen in 35 (10.6%) patients. Treatment success were denoted in 161(48.8%) patients, where their symptoms completely resolved. In addition, a total of 40 (12.1%) HMF patients began to gain weight. However, postoperative symptoms existed in 41 (12.4%) patients with dysphagia, 32 (9.7%) patients with GERD, and 6 (1.8%) children with vomiting.

Among patients in HM group, 45 (56.3%) of them showed absence of symptoms and partial improvements were seen in 3 (3.8%) patients. Unfortunately, recurrent symptoms occurred in 3 (3.8%) patients, dysphagia still remained in 20 (25.0%) patients, and 12 (15%) patients reported GERD symptoms. Furthermore, 17 (21.3%) patients reported higher body weight compared to before the treatment.

(Table 4)

Table 3. Study characteristics of included studies

Author	Study design	Study period	No. of patients	Intervention		Age	Gender
				HM	HMF		
Yu <i>et al.</i> (2019) ¹⁰	Cross-sectional	2010 - 2017	30	0	30	13.6 ± 3 ^a	18 males, 12 females
Vandewalle <i>et al.</i> (2018) ¹¹	Case series	January 2007-December 2016	26	0	26	14.4 (11.6-15.5) ^a	16 males, 10 females
Vaos <i>et al.</i> (2008) ¹²	Retrospective cohort	January 1991-December 2005	15	15	0	9.5 (6.0-13.0) ^b	5 males, 11 females ^c
Garzi <i>et al.</i> (2007) ¹³	Prospective cohort	January 1997-October 2005	12	0	12	11 (3.5-16.0) ^a	7 males, 5 females
Saliakellis <i>et al.</i> (2017) ¹⁴	Cross-sectional	January 1995-December 2012	40	2	38	10 (3.2-17.4) ^{b, d}	21 males, 27 females ^{c, d}
Altokhais <i>et al.</i> (2016) ¹⁵	Cross-sectional	January 2004-November 2015	6	0	6	7 (2.0-12.0) ^a	2 males, 4 females
Erginel <i>et al.</i> (2016) ¹⁶	Case series	1991-2013	20	0	20	3.34 (0.58-17.0) ^{a, d}	13 males, 9 females ^{c, d}
Zagory <i>et al.</i> (2016) ¹⁷	Case series	September 2004-August 2014	19	1	18	11.6 (0-17) ^{b, d}	14 males, 9 females ^{c, d}
Smits <i>et al.</i> (2015) ¹⁸	Cross-sectional	January 1990 – December 2013	41	15	26	11.9 (9.3 – 13.8) ^a	52 males, 35 females ^{c, d}
Caldaro <i>et al.</i> (2015) ¹⁹	Retrospective cohort	February 2009-December 2013	9	0	9	10.7 (2-16) ^a	6 males, 3 females
Pachl <i>et al.</i> (2014) ²⁰	Retrospective cohort	May 1999- May 2013	28	18	10	13 (3.2- 17.4) ^a	13 males, 15 females
Esposito <i>et al.</i> (2013) ²¹	Case series	June 2000 – June 2012	31	0	31	8.4 (5 – 14.9) ^a	18 males, 13 females
Tannuri <i>et al.</i> (2010) ²²	Cross-sectional	2000-2009	15	0	15	12.0 (9.0-17.0) ^a	7 males, 8 females
Jung <i>et al.</i> (2010) ²³	Case series	1990-2007	17	0	17	7 (0.3- 17) ^a	12 males, 10 females ^c

Corda <i>et al.</i> (2010) ²⁴	Case series	January 1998- June 2008	20	20	0	12 (5-15) ^a	13 males, 7 females
Pastor <i>et al.</i> (2009) ²⁵	Cross-sectional	July 1981- June 2007	20	2	18	12.4 ± 4.8 ^{a, e}	5 males, 5 females ^c
Askegard-Giesmann <i>et al.</i> (2009) ²⁶	Case series	1999-2005	26	1	25	15 (4-18) ^a	15 males, 11 females
Zhang <i>et al.</i> (2009) ²⁷	Case series	May 1993- October 2005	9	6	3	10.3 (3.0-14.4) ^b	6 males, 7 females ^c
Grabowski <i>et al.</i> (2016) ²⁸	Case series	1997-2014	11	0	11	13 (6-17) ^a	7 males, 4 females
Ashraf <i>et al.</i> (2014) ²⁹	Case series	January 2002- December 2007	10	0	10	8 (infants), 2 (4-year-old) ^f	6 males, 4 females
Adikibi <i>et al.</i> (2009) ³⁰	Case series	2000-2007	5	0	5	12.1 (9.3-14.9)	4 males, 1 female

HM: Heller's myotomy alone; HMF: Heller's myotomy with fundoplication

NR: Not reported

^a., Age at surgery

^b., Age at diagnosis

^c., Data includes excluded patients

^d., Data of all patients of the study, which also includes those who received initial treatments besides Heller myotomy and fundoplication.

^e., Data of patients undergoing Heller's myotomy as initial intervention only

^f., Age only reported in terms of infants and 4 years old children

Table 4. Postoperative outcomes of included studies with HM only or HMF patients only

Author(s)		Achalasia symptoms				Dysphagia	GERD	Vomiting	Gained weight
		Relapse	Improvement		Asymptomatic				
			Dysphagia	GERD					
Yu <i>et al.</i>	HMF	NR	NR	19	10 ^p	NR	5	NR	
Vandewalle <i>et al.</i>	HMF	NR	16	13	NR	10 ^p	7	NR	NR
Garzi <i>et al.</i>	HMF	NR	N/A	12	NR	NR	NR	12	
Saliakellis <i>et al.</i>	HMF	NR	NR	15 ^a	NR	11	NR	NR	
Altokhais <i>et al.</i>	HMF	NR	1	5	NR	NR	NR	NR	
Erginel <i>et al.</i>	HMF	NR	N/A	20	NR	NR	NR	NR	
Zagory <i>et al.</i>	HMF	NR	NR	14	5	NR	NR	NR	
Caldaro <i>et al.</i>	HMF	NR	NR	NR	2	1	NR	NR	
Esposito <i>et al.</i>	HMF	NR	NR	30	5	NR	NR	NR	
Tannuri <i>et al.</i>	HMF	NR	NR	NR	2	-	NR	NR	
Jung <i>et al.</i>	HMF	NR	4	10	NR	NR	NR	NR	
Pastor <i>et al.</i>	HMF	NR	NR	6 ^b	3 ^b	NR	1 ^b	NR	
Askegard-Giesmann <i>et al.</i>	HMF	7	NR	NR	NR	1	NR	NR	
Grabowski <i>et al.</i>	HMF	4	NR	6	4	-	NR	11	
Ashraf <i>et al.</i>	HMF	NR	N/A	10	NR	-	NR	10	
Adikibi <i>et al.</i>	HMF	NR	1	4	NR	NR	NR	NR	
Vaos <i>et al.</i>	HM	NR	NR	10	1 ^p , 13 ^o	NR	NR	NR	
Corda <i>et al.</i>	HM	NR	NR	15	5	-	NR	NR	
Smits <i>et al.</i>	HM	3	NR	NR	NR	5	NR	NR	
	HMF	1	NR	NR	NR	9	NR	NR	
Pachl <i>et al.</i>	HM	NR	NR	17	NR	1	NR	17	
	HMF	NR	NR	7	NR	3	NR	7	
Zhang <i>et al.</i>	HM	NR	3	3	1	2	NR	NR	
	HMF	NR	NR	3	-	-	NR	NR	

HM: Heller's myotomy only; HMF: Heller's myotomy along with fundoplication

N/A: Not applicable; NR: Not reported; -: No patients in the category

GERD: Gastroesophageal reflux disease

^p., Persistent dysphagia; ^o., Occasional dysphagia

^a., Data of patients undergoing Heller's myotomy as initial intervention only

^b., Data of patients undergoing Heller's myotomy as their last treatment

Secondary Outcomes

Overall, no deaths were seen among the subjects. The length of hospitalization of HMF patients (4.63 (2.38-14.13) days) is longer compared to those of HM patients (3.5 (2.0-5.0) days). A total of 120 (36.4%) out of 330 patients were able to be followed up to a range mean of 0.25 to 4.42 years postoperatively. In **Table 5** it can be seen that complications within HMF patients were intraoperative mucosal perforation (n= 18 (5.5%)), postoperative gastric perforation (n= 1 (0.3%)), persistence of painful symptoms (n= 3 (0.9%)), dumping syndrome (n= 3 (0.9%)), and inhalation pneumopathy (n= 1 (0.3%)). Other adverse effects include gas bloat syndrome (n= 1 (0.3%)), aspiration during induction of anesthesia (n= 1 (0.3%)), pneumonia (n= 2 (0.6%)), and retrosternal pain (n= 2 (0.6%)). Not only that, in eight cases (2.4%) the Nissen fundoplication was overly tight.

There were a smaller number of complications among HM patients, namely four (5.0%) patients with perforation of the esophageal mucosa during the surgery, one (1.3%) patient who developed esophagitis, and one (1.3%) with pneumonia. Infection also occurred in two (2.5%) patients, one of them was located in the chest and the other one was a local infection of the wound. The average follow-up period was similar to that of HMF patients, which was 0.83 to 5 years. The data of Vaos et al. were excluded from the calculation of the follow-up duration as he provided only the range of years elapsed after the surgery without the average. The included studies managed to follow 32 HM patients.

Table 5. Characteristics of the included studies in regard to follow-up and complications

Author		Complication		Follow-up		Length of hospital stay (days)
		IMP	Others	Duration	No. of patients followed	
Yu <i>et al.</i>	HMF	NR	NR	3.6 ± 2.1	12	NR
Vandewalle <i>et al.</i>	HMF	1	1 ^a	0.81 (0.29-1.75)	NR	NR
Garzi <i>et al.</i>	HMF	1	3 ^b	NR	12	NR
Saliakellis <i>et al.</i>	HMF	NR	NR	NR	NR	NR
Altokhais <i>et al.</i>	HMF	-	-	2 (0.5-11)	NR	3.5 (2-7)
Zagory <i>et al.</i>	HMF	1	NR	NR	NR	6.5 (1-40)
Caldaro <i>et al.</i>	HMF	1	NR	2.58 (1.08-5.25)	NR	6 (3-18)
Esposito <i>et al.</i>	HMF	3	NR	0.75-13	31	4 (3-8)
Tannuri <i>et al.</i>	HMF	NR	NR	2.69 (0.17-8)	NR	2.5 (1-4)

Jung <i>et al.</i>	HMF	NR	8 ^c	0.5	17	NR
Pastor <i>et al.</i>	HMF	3	1 ^d	NR	20	NR
Askegard-Giesmann <i>et al.</i>	HMF	2	1 ^e	1.7 (0-6.21)	NR	3.5 (1-17)
Grabowski <i>et al.</i>	HMF	2	NR	2.5 (1-10)	10	8 (5-13)
Ashraf <i>et al.</i>	HMF	NR	NR	0.25	10	NR
Adikibi <i>et al.</i>	HMF	-	-	4.42 (0.13-7.58)	5	3 (3-6)
Vaos <i>et al.</i>	HM	NR	3 ^f	5-15	7	4 (3-6)
Corda <i>et al.</i>	HM	3	NR	5.00 (0.67-9.50)	20	3 (1-5)
Smits <i>et al.</i>	HM	-	1 ^g , 1 ^h	NR	NR	NR
	HMF	4	2 ^g , 2 ⁱ , 1 ^h	NR	NR	NR
Pachl <i>et al.</i>	HM	1	NR	0.83 (0-5)	25	3 (1-8)
	HMF	-	NR			
Zhang <i>et al.</i>	HM	NR	NR	1.27 (0.17- 4)	5	NR
	HMF	NR	NR		3	NR

NR: Not reported; -: No patients in the category

^a., Postoperative gastric perforation

^b., Patients reported persistence of painful symptoms

^c., Other complications consists of 3 Dumping syndrome patients, 1 patient with inhalation pneumopathy, and 4 patients that had their Nissen fundoplication too tight

^d., Gas bloat syndrome

^e., Aspiration during induction of anaesthesia

^f., Three patients consisting of 1 patient with chest infection, 1 with wound infection, and one with oesophagitis.

^g., Pneumonia

^h., Oesophagectomy

ⁱ., Retrosternal pain

Discussion

Achalasia is a rare motility disorder, especially among children. In managing achalasia, surgical intervention was said to offer a more long-lasting improvements of the symptoms compared to pharmacological treatments. One mode of surgery is HM, which although known as the gold-standard it also has a risk of triggering GERD. To solve the reflux symptoms, a technique of wrapping the fundus of the stomach around the esophagus called fundoplication might be used. However, until now it is still unclear whether the benefits of using fundoplication outweigh its risks. Thus, we aim to review whether fundoplication leads to better improvement in achalasia symptoms along with less postoperative GERD compared to HM alone.

From **Table 4** it can be seen that there were less asymptomatic patients in the HM group (n= 45) compared to HMF (n= 161). However, the number of cases was not

representative of the actual proportion of asymptomatic patients, as the number of patients within each group were different. Therefore, calculations of the percentage were deemed to be more appropriate. After dividing the number of asymptomatic patients reported per children in each group, there was a higher percentage of asymptomatic HM patients (56.3%), compared to HMF (48.8%).

The difference in the number of patients with no persisting symptoms after the operation in both groups can be explained by a possible technical error of the fundoplication, in which it was done too tightly, hence created obstructing symptoms of the esophagus and hinder the recovery.

The difference in the number of asymptomatic patients can also be explained by a higher proportion of patients in the HMF group (33.3%) that underwent preoperative treatments compared to HM (8.8%). A study done by Portale et al. mentioned that patients who had prior treatments with BT injection were less likely to be asymptomatic than those who had not.³¹ From all of those studies, 11 HMF patients had previous BT injection while there were no HM patients who underwent treatment with BT.

There was also a difference in the length of follow-up, where the mean was longer in HM patients (0.83-5 years) than HMF (0.25-4.42 years), allowing more asymptomatic HM patients to be noted by the research. Furthermore, only 120 (36%) HMF patients were able to be followed-up as compared to 32 (40%) in HM patients. This finding made it unclear whether the patients that were lost to follow up had an improved condition or not.

Both groups had a similar rate of achalasia symptoms relapse, with 3.8% of patients in the HM group and 3.6% in the HMF group. According to Askegard-Giesmann et al. and Weche et al., the presence of relapse cases among the patients was caused by incomplete myotomy in most cases.²⁶ As stated above, an overly constricting fundoplication might also contribute to the symptoms relapse in HMF patients, as it adds to the obstruction of the LOS. This can be seen in **Table 5**, where indeed, there were four cases among HMF children where the fundoplication was done with excessive tightness. Reflux symptoms can be triggered in children with no fundoplication but had an adequate myotomy, which can potentially induce stricture due to peptic stricture of the LOS.³²

On the other hand, partial improvements were seen in more HMF patients (10.6%) as compared to HM (3.8%). This is consistent with the findings of Li et al., although

it was said that the improvement of symptoms post-fundoplication was more specific to reflux-related symptoms such as heartburn and regurgitation.³³

The rate of persistent or occasional dysphagia was reported approximately twice as much in 20 HM patients (25%) as in 41 HMF patients (12.4%). In order to manage the persistent symptom of dysphagia, esophagectomy might be considered. However, there were a probability of esophageal resection to cause anastomotic leak, as shown in a study by Devaney et al.³⁴ Therefore, it was suggested by Fernandez-Ananin et al. that esophagectomy should be performed only when the more conservative treatment has failed.³⁵ In the case of fundoplication types, Frazzoni et al. suggested the use of partial fundoplication instead of total in order to prevent postoperative dysphagia.⁹

GERD occurred in 12 HM patients (15%) and 32 HMF patients (9.7%). The higher percentage of GERD among patients with no fundoplication was as expected, as the aim of using fundoplication was to prevent reflux. In addition, Moore et al. had stated that laparoscopic fundoplication is the gold standard in treating GERD.⁷ However, as there was only as much as 5.3% reduction in the incidence of GERD, it suggests that the benefits of using fundoplication was limited.

Both groups in this study had cases of complications. Complications occurred in a similar rate in HMF children (n= 40 (12.1%)) and among HM patients (n= 8 (10.0%)). Madiwale et al. found out that fundoplication in children was associated with a higher incidence of complications, which supported the slightly higher percentage of complications in HMF patients.³⁶ In addition, it was found that the most common complication in both groups in our study were intraoperative mucosal perforation (IMP) during myotomy. It is important to take into account that HMF children had more preoperative surgical and/or pharmacological interventions, which might have impacted the condition of the patients and made them prone to developing complications.

The limitation of this study is that there was a presence of numerous confounding factors, such as duration of surgery, preoperative treatments, variable patient ages, duration of follow-up. However, this happened due to the included papers being cross-sectional, cohort studies, case control, and case series. Another limitation is the significant difference in the number of patients within both groups, which was inevitable as the included papers were those that suit the eligibility criteria the most. A larger sample size is needed to have a significant number of patients in the study; however, it was unable to be done as most of the studies were single centered as well as achalasia being a rare disease among children. Another limitation was the incompleteness of several data from the papers, however, the most necessary data which was the primary and secondary endpoints were able to be retrieved from all

studies. A potential source of bias of this review was that the literature search was not performed by looking at the references of articles on relevant topic, and grey literatures. However, the search strategy was performed on four databases and developed through the help of an expert librarian. Another potential bias was missing information of the studies, which was stated in the table of results. We were unable to retrieve the full text of 7 articles and exclusion of 4 non-English papers were performed, which might add to potential bias of this paper.

Conclusion

Our results suggested that the HM group was superior to HMF in terms of the primary outcome of symptom resolution, with only a slight improvement of GERD symptoms in children who had fundoplication. Furthermore, patients with fundoplication in our study had also shown more complications intra and postoperatively. Thus, it is important for surgeons to carefully and precisely perform the fundoplication, especially to prevent an excessively tight wrapping and perforation due to the injury the oesophageal mucosa. Future research that uses prospective cohort studies should be performed, as it is able to calculate incidence. RCTs could also be performed through conducting an international multicenter study to gather sufficient number of achalasia patients. Future studies should have only a minimal amount of surgeon who perform the surgeries, in order to prevent the difference of the surgeon's skills to be the confounding factor.

Conflict of Interest

None declared.

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