Esophageal Motility Outcome after Nissen Fundoplication: A Systematic Review and Meta-Analysis

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Abstract

Background: Gastroesophageal reflux disease (GERD) is a very prevalent disease. The Montreal consensus conference in 2006 defined GERD as "a condition which develops when the re-flux of gastric contents causes troublesome symptoms and/or complications". The pathophysiology of GERD is multifactorial and complex but revolves around an incompetent esophagogastric junction (EGJ) as an anti-reflux barrier, in the form of transient lower esophageal sphincter relaxations (TLESR) and/or a hypotensive EGJ.

Aim of Study: To evaluate the efficacy of laparoscopic surgeries with regard to esophageal motility and determine a clear indication for these interventions. Additionally, we will compare between preoperative and postoperative manometer results.

Patients and Methods: This systematic review and meta-analysis was conducted by careful following of the Cochrane handbook for systematic reviews interventions and the results were described according to the Preferred Reporting Items for Systematic reviews and Meta-analysis (PRISMA) statement. The following electronic databases were searched till 2022: PubMed, Medline, Embase, Cochrane Library, Springer link, databases. A manual search was also performed to identify trials in the reference lists of the articles acquired. A search strategy using disease-specific terms (e.g., gastro-esophageal reflux disease), management-specific terms (e.g., laparoscopic antireflux fundoplication), and terms related to surgical procedures (Nissen) were adopted.

Results: The forest plot meta-analysis shows that Nissen fundoplication significantly reduce the maximum diameter of the EGJ. Also it reduces significantly the cross-section area (CSA) at the EGJ, which means successful fundoplication that permit less refluxate through the EGJ. Also Distensibility index (DI) which can be calculated by dividing the cross-section area of the EGJ (CSA) by the infra-bag pressure at the EGJ. It was found that the distensibility index decreased significantly after Nissen fundoplication than that before fundoplication The

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decrease of the Distensibility index means more tight fundoplication that controlling reflux.

Conclusion: This meta-analysis concluded that Nissen fundoplication increase significantly the LESP which control most of the reflux symptoms as it decreases significantly the regurgitation and heart burn symptoms. Also, it found that it significantly decreases the use of proton pump inhibitors and improve life mode of the patient. But it does not significantly change the dysphagia symptoms especially in the early postoperative period. This study promotes much research on the EndoFLIP maneuver during the operation just in the time before insufflation and after performing the wrap as this Endo FLIP assists mostly adjusting the tightness of the wrap.

Key Words: Gastroesophageal reflux disease — Transient lower esophageal sphincter relaxations — Cross section area.

Introduction

GASTROESOPHAGEAL reflux disease (GERD) is a very prevalent disease. Population studies have repeatedly shown GERD-related symptoms in a significant proportion of adults. The Montreal consensus conference defined GERD as "a condition which develops when the re-flux of gastric contents causes troublesome symptoms and/or complications" [1]. However, this definition did not include details of the pathophysiology of the disease and its implications for treatment. The Brazilian consensus conference considered GERD to be "a chronic disorder related to the retrograde flow of gastro-duodenal contents into the esophagus and/or adjacent organs, resulting in a spectrum of symptoms, with or without tissue damage" [2]. This definition recognizes the chronic character of the disease and acknowledges that the refluxate can be gastric and duodenal in origin, with important implications for the treatment of this disease [3].

Esophageal manometry is the gold standard test to assess esophageal function, and motility disorders are classified based on manometric findings [4].

Usually, the treatment of GERD includes medical treatment with proton pump inhibitors (PPIs) which proved to be effective in healing lesions and improving symptoms of GERD in most cases, although up to 40% of GERD patients do not respond adequately to PPI therapy [5,6]. In these cases, surgical treatment is introduced.

One of the surgical solutions that gained popularity is laparoscopic management. The laparoscopic transabdominal approach is preferred over transthoracic and open abdominal approaches which are reserved for patients who needs revision of their former anti-reflux operations [7]. Laparoscopic repair has the advantage of shorter hospital stay, decreased pain, low incidence of postoperative wound infections and abdominal wall hernia formation. Furthermore, surgeons could see the hiatal structures in a magnified fashion [8].

In patients with GERD, assessment of esophageal motor function contribute significantly in guiding treatment strategy, particularly when esophageal symptoms do not improve with PPI therapy, and when surgical intervention is considered [9]. Hence, our study focuses on motility outcome.

In the literature, the effect of laparoscopic anti-reflux surgery on esophageal motility is incompletely understood, with no clear indications regarding the use of these techniques [10,11].

Therefore, in this article we chose to assess the impact of laparoscopic surgery on esophageal motility in order to determine the efficacy of this approach and to provide objective evidence regarding the advantage and disadvantages of laparoscopic approach.

Aim of the work:

We aim in this review to evaluate the efficacy of laparoscopic surgeries with regard to esophageal motility and determine a clear indication for these interventions. Additionally we will compare between preoperative and postoperative manometer results.

Patients and Methods

This systematic review and meta-analysis was conducted by careful following of the Cochrane handbook for systematic reviews interventions and the results were described according to the Preferred Reporting Items for Systematic reviews and Meta-analysis (PRISMA) statement [12].

The following electronic databases were searched till 2022: PubMed, Medline, Embase, Cochrane Library, Springer link, databases. A manual search was also performed to identify trials in the reference lists of the articles acquired. A search strategy using disease-specific terms (e.g., gastro-esophageal reflux disease), management-spe-

cific terms (e.g., laparoscopic antireflux fundoplication), and terms related to surgical procedures (Nissen) were adopted.

Inclusion criteria:

Include the studies which have patients with GERD who are treated with Nissen fundoplication, and esophageal motility improvement will be assessed and compared to the preoperative status. The exclusion criteria are incomplete outcome data, selective outcome reporting with high risk of bias, non-English studies, animal or cadaver studies, reviews, books chapters, letters to editors and papers with overlapped data-set (studies for which raw data could not be extracted to obtain pooled results).

Data extraction:

A standardized extraction form will be prepared by Microsoft excel. Two independent reviewers will extract the following data from each of the included studies: Study characteristics as, first author name, year of publication, country of origin, and duration of the study. Participants baseline characteristics, as age, gender, history of symptoms and use of PPIs, and also outcome results mainly esophageal manometry. Risk of bias domains.

Statistical analysis:

Data extracted from eligible studies were integrated with Review Manager 5.4 provided by the Cochrane Collaboration, following the recommendation of The Cochrane Collaboration and Quality of Reporting of Meta-analyses guidelines [12]. Outcomes reported by 2 or more studies were pooled in the meta-analysis. Dichotomous and continuous outcomes were presented as risk ratio (RR) and weighted mean difference respectively. Results were pooled using standardized mean difference (SMD) if a continuous outcome was reported by different scales. Dichotomous outcomes were pooled using the Mantel-Haenszel method, while continuous outcomes were pooled using the inverse variance method. The fixed-effects model was used if heterogeneity was absent (x² test, p>.1 and I²<50%). If excessive heterogeneity was present, data were first rechecked, and the random-effects model was used when heterogeneity persisted. Subgroup analysis was performed to assess the impact of follow-up duration. Funnel plots were used to identify the presence of publication bias.

Results

After screening of studies according to inclusion and exclusion criteria, and only studies in which preoperative and postoperative manometry are included, 1 RCT [13] and 8 retrospective studies [14-211 were identified, including 661 patients, of whom 337 (50.98%) underwent laparoscopic Nissen fundoplication (LNF), and have done manometry (either conventional method or with high resolution manometry HRM) preoperative and postoperative.

Many studies were excluded as extraction of data from these studies was impossible, aggregate data from multiple techniques and lack of desired data (Fig. 1). Included studies were published between 2014 and 2021, with period of follow-up range from 6 months up to 55 months.

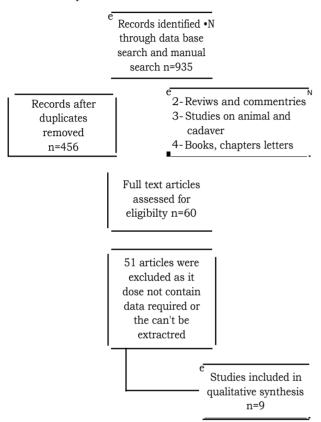


Fig. (1): A flowchart showing the process and result of studies screening and selection.

Table (1) shows the basic characteristics of the included studies as regard the main author, country, year of publication, time of study and time of follow up, while Table (4) shows number of patients, mean age, percentage of each gender, and body mass index BMI of patients in each study.

Table (3) shows some details about the operative procedure and the perioperative morbidity. As regard the mortality, all authors report that there was no mortality in their studies which means that Nissen fundoplication is a safe procedure. Also, the hospital stay was within one week on average. Also, the perioperative complication.

I- *Primary outcome (Motility outcome):*

The primary outcome is concerned with the effect of Nissen fundoplication on the esophageal motility and how it could change the parameters for benefit of improving GERD. Esophageal motility is so complicated subject, and it is hard to find a group of studies that follow the same method and give the same name of parameters. Also, there are two ways for esophageal manometry, the traditional old

one which record the conventional line tracing and the new technique which is called high resolution manometry (HRM). Another modification was introduced using the functional lumen imaging probe (endo FLIP) that has been applied to assess lumenal distensibility in the esophageal lumen and at EGJ, also it could measure the pressure within the esophageal lumen and EGJ. In this meta-analysis we will compare 3 items belonging to the end FLIP (distensibility of the EGJ, CSA at the EGJ and distensibility index) and one parameter belong to the conventional or high resolution manometry which is the lower esophageal sphincter pressure (LESP).

A- Distensibility at the esophagogastric junction (EGJ):

Only two studies [17,20] measure the distensibility differences between per-fundoplication and post fundoplication.

1-Minimum esophageal diameter, (Dmin):

The forest plot meta-analysis shows a significant difference between minimum distensibility at the EGJ before and after fundoplication as the maximum value before fundoplication was 7 7mm while it becomes 6.3 after fundoplication at the EGJ (p-value <0.0001, SMD is 0.68, 95% CI between 0.40 to 0.97), and there is no heterogeneity in the data collected (Fig. 2).

2- CSA of the EGJ:

Estimation of the cross-section area (CSA) at the EGJ pre and post fundoplication. Forest plot meta-analysis found that there is significant difference between the cross-section area of the EGJ, as it is significantly decrease in post fundoplication which means successful fundoplication that permit less refluxate through the EGJ (p-value <0.0001, CI between 8.70 to 19.05, MD is 13.87 with zero heterogeneity) (Fig. 3).

3- Distensibility index:

Distensibility index (DI) can be calculated by dividing the cross-section area of the EGJ (CSA) by the intra-bag pressure at the EGJ. The mean minimum CSA and intra-bag pressure were calculated over a 20-s interval for each measurement and used for determining DI. The decrease of the distensibility index means more tight fundoplication that controlling reflux on performing meta-analysis forest plot for studies which record distensibility index [17,20] it was found that the distensibility index decreased significantly after Nissen fundoplication than that before fundoplication (with p-value <0.0001, MD = 2.37, 95% CI between 1.71 to 3.04) which mean that Nissen fundoplication significant control on the reflux of gastric content (Fig. 4).

B- Lower esophageal sphincter pressure (LESP):

On doing Meta analysis forest plot for comparison of LESP in the pre and post Nissen fundo-

plication, there are 7 studies which record pre and postoperative manometry using either conventional method or using high resolution manometry. These studies are [13-16,19-21]. They estimated that there is significantly increase in the post Nissen fundoplication LESP than before Nissen fundoplication (p—value = 0.002, SMD = -1.26, 95%CI between -2.38 to -1.34). The preoperative LESP range from 7.7 ± 4.7 to 15.2 ± 9.4 mm Hg While in the postoperative state, it was ranging between 13.8 ± 4.7 to 24.8 ± 6.4 . (Fig. 5).

II- Secondary outcome:

1-De meesters score:

It is a composite score of the acid exposure during a prolonged ambulatory PH monitoring, it is used to categorize patients as GERD+ OR GERD- and it is estimated that the value below 14.7 is considered negative for GERD. In this meta-analysis only two studies that record their de Meesters score [13,21]. The forest plot of this meta-analysis shows that de Meesters score decreased significantly post fundoplication than that it was in the pre-fundoplication period (p-value <0.00001, MD29.68, and 95% CI between 24.46 to 34.90). There was no heterogeneity in the data of the studies that is recorded. In the preoperative time, the minimum result was 35.22±11.74 while the minimum result obtained in the postoperative state was 5.55±2.08 (Fig. 6).

2- Dysphagia:

There is insignificant difference in percentage of dysphagia between preoperative and postoperative as (the p-value=0.06, OR 1.73, 95% CI between 0.98 to 3.05). Although the percentage of postoperative dysphagia (19.7%) less than that of the preoperative percentage (29.6%), but still insignificant results. However, this percentage of postoperative dysphagia considered as high record and it may be due several causes as postoperative edema in wrap and this type of dysphagia resolves after some weeks of the operation. Another cause of the dysphagia is tight wrap which could be treated either by endo-

scopic dilatation or redo of the operation changing it into Toupet 270° fundoplication. For this reason, most surgeons doing Nissen fundoplication use bogie (about 52-56 french) to avoid this complication. In this meta-analysis 7 of the included studies used bougie during fundoplication (Fig. 7).

3- Regurgitation:

There are 3 studies record the effect of Nissen fundoplication on regurgitation [13,14,21]. Forest plot meta-analysis of these results explains that there is significant decrease in regurgitation symptoms after Nissen fundoplication (p-value <0.00001, OR 42.14 and the 95% CI between 16.34 to 108.68). The heterogeneity in the recorded data is 74% and the preoperative percentage of regurgitation was 83.3% which decrease to 10.8% in the postoperative period (Fig. 8).

4- Heart burn:

Also the same three studies which record regurgitation, describe heart bum before and after fundoplication [13,14,21]. Forest plot meta-analysis of the results shows that heart bum symptoms significantly decrease in the post fundoplication than that was before fundoplication (p-value <0.00001., OR=21.05., 95% CI between 9.97 to 44.47). There is low heterogeneity (33%) and the percentage of heart bum symptoms before the operation is 83.3% while after the operation it falls to 18.3% (Fig. 9).

5- Proton pump inhibitors (PPi) use:

There only two studies which record the use of proton pump inhibitors pre- and post-fundoplication. Forest plot meta-analysis of that results shows that there is significant difference in the use of **PPI** as there significantly decreased use of **PPI** after fundoplication than before fundoplication (p-value <0.00001, ORIS 213.20., 95% CI between 60.92 to 746.11, but the heterogeneity is equal to 69%). The percentage of **PPI** use in the preoperative period is about 97% which drops to 7.7% in the postoperative period (Fig. 10).

Table (1): Table of studies characteristics.

Study	Туре	Country	Period of study
Katada et al. [15]	Prospective cohort study	Japan	
Shedeed et al. [21]	Prospective study	Egypt	June 2019-June 2021
He et al. [19]	Prospective study	China	August 2018-June 2019
Wang et al. [13]	Randomized control trail	China	Jan 2010-Jan 2013
De Haan et al. [17]	Prospective trial	USA	September 2013-Aug 2015
Turner [20]	Retrospective	USA	2014- 2018
Marano et al. [14]	Prospective	Italy	2007-2010
Mello et al. [16]	Prospective	USA	2007-2014
Kapadia et al. [18]	Retrospective study	USA	June 2011-December 2014

Table (2): Patients characteristics.

Study	No. of patients	Mean age	Gender	BMI	HH presence
Wang et al. [13]	43	57.0±13.2	M/F 20/23	23.5±2.7	43/51
					84.3%
He et al. [19]	52/51	53.2±11.3	36/15	22.9 ± 3.7	-
Marano et al. [14]	13	Median 67 years (range 37-71)	M/F 5/8	=	-
Turner et al. [20]	43	57.1±11.5	14/29	31.3±4.5	-
			28 with Nissen		
Mello et al. [16]	68	53.9±1.8	23/45	_	52/68
March Carlos Control					67.47%
Shedeed et al. [21]	40	32.35±9.98	15/25	24.51±1.92	
De Han et al., 2017	75/45 nissen	55.2±13.9	26/49	28.9 ± 4.7	6
Katada et al. [15]	35-33	65.6	12/23	-	35/35
Jakon Leitere Sabria	10 nissen				
Kapadia et al. [18]	146/52	4	5 <u>4</u>	<u>-</u>	100%

Table (3): Some details about surgical procedure.

Study	Operative time/min	Use of bougie	Use of mesh	Intraoperative Post operative Hospital complications stay			
Marano et al. [14]	128.3±16.3	Endoscope	Yes when required	2 Surgical emphysema 2 Pleural effusion	5 (4-7)		
				No mortality			
Katada et al. [15]	=	54-F bougie	No	3 with severe dysphagia one need dilation	=		
Mello et al. [16]	3 <u>4</u>	<u> </u>	=				
Wang et al. [13]	114.4±26.9	A 32-Fr bougie	Yes when hiatal hernia is more than 5.6 cm	7 patients	6.1±1.2		
De Haan et al. [17]		Yes	-		12		
Kapadia et al. [18]		54-56 Fr	-	Dysphagia	_		
Turner et al. [20]	<u>-</u> :	56-60 Fr	-	31 8	-		
He et al. [19]	55	No	Yes when hernia 3 cm	1 dyspnea 1 dysphagia relied by dilatation 3 diarrhea	3.0±1.5		
Shedeed et al. [21]	-	Yes	No				

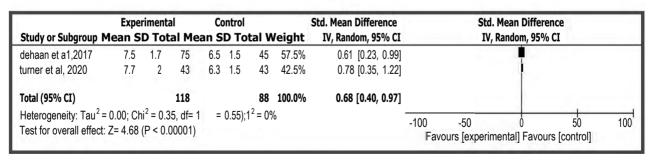


Fig. (2): Forest plot of comparison: Dmin of EGJ Preoperative and postoperative, outcome.

pre fundoplication				post fu	ndoplica	tion		Mean Difference	Difference Mean Difference			се	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		I\	/, Fixed, 95%	CI	
dehaan et a1,2017	45.9	21.7	75	32.8	13.1	45	69.0%	13.10 [6.87, 19.33]					
turner et al, 2020	49.6	25.9	43	34	17.2	43	31.0%	15.60 (6.31, 24.89]					
Total (95% CI)			118			88	100.0%	13.87 [8,70, 19.05]					
Heterogeneity: Chi': Test for overall effect:		•	,.	:0%					-100 Favo	•50 ours [experim	0 lental] Favoui	50 rs [control]	100

Fig. (3): Forest plot of comparison: 8 CSA of the EGJ, outcome: 8.1 CSA of the EGJ.

	PREOP	ERATI\	/E	POST 0	PERATI	VE		Mean Difference		Me	an Difference		
Study or Subgroup Mean SD Total			Total	Mean	SD T	otal V	Veight IV	, Fixed, 95% CI	IV, Fixed, 95% CI				
dehaan et a1,2017	3.4	3.4	75	1.4	0.8	45	68.9%	2.00 [1.20, 2.80]			1		
turner et al, 2020	4.6	3.9	43	1.4	0.9	43	31.1%	3.20 [2.00, 4.40]					
Total (95% CI)			118			88	100.0%	2.37 [1.71, 3.04]					
Heterogeneity: Chi ² = Test for overall effect		•	,	² = 62%					-100 Fav	-50 ours [experime	0 ental] Favours [c	50 ontrol]	100

Fig. (4): Forest plot of comparison: 10 DI Of the EGJ, outcome: 10.1 New Outcome.

	Expe	Experimental			Control		;	Std. Mean Difference	Std. Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight I	V, Random, 95% Cl		IV, Rando	m, 95% CI	
he et al, 2021	9.7	4.3	51	13.8	4.7	51	17.4%	-0.90 [-1.31, -0.50]				
katada et al, 2014	11.1	4.5	10	17.3	5.9	10	14.3%	-1.13 [-2.09, -0.17]		•		
marano et al, 2014	93	2.1	13	21.2	1.6	13	0.5%	37.25 [26.23, 48.26]				
mello et al, 2016	13.8	1.7	39	16.2	1.8	39	17.1%	-1.36 [-1.85, -0.86]		•		
shedeed et al, 2021	10.41	4.79	40	20.2	3.86	40	16.7%	-2.23 [-2.79, -1.67]		•		
urner et al, 2020	15.2	9.4	36	24.8	6.4	36	17.0%	-1.18 [-1.68, -0.68]		•		
wang et al, 2015	7.7	4.7	43	18.74	6.91	41	17.0%	-1.86 [-2.38, -1.34]				
Total (95% CI)			232			230	100.0%	-1.26 [-2.04, -0.48]				
Heterogeneity: Tau'=	0.87; Ch	i ² = 65	36, df	= 6 (P <	0.0000)1);1 ² =	91%		-100	-50	. 50	10
Test for overall effect:	Z= 3.16	(P = 0.0)	002)							ים urs [experimental)) 50 Favours [control)	10

Fig. (5): Forest plot meta-analysis of the LESP pre and post fundoplication.

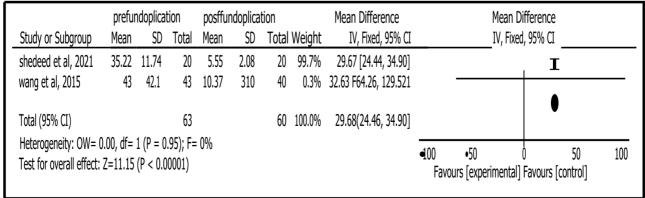


Fig. (6): Forest plot show comparison between pre and postoperative de meesters score.

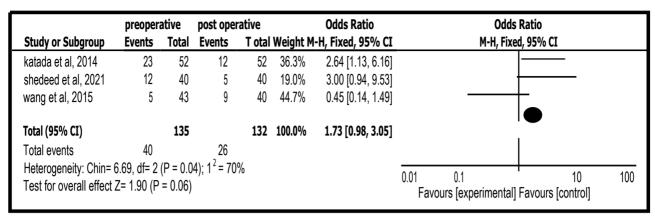


Fig. (7): Forest plot meta-analysis of dysphagia pre and post fundoplication.

	preoperative		postopera	tive		Odds Ratio	Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fi	xed, 95% CI	
wang et al, 2015	41	43	2	40	5.8%	389.50 [52.24, 2904.17]				
shedeed et al, 2021	35	40	7	40	52.6%	33.00 [9.53, 114.29]				
marano	4	13	1	13	41.6%	5.33 [0.51, 56.24]				
Total (95% CI)		96		93	100.0%	42.14 116.34, 108.68]				
Total events	80		10							
Heterogeneity: Chi ² = Test for overall effect:				6			0.01 Fav	0.1 ours [experimenta	10 al] Favours [control]	100

Fig. (8): Forest plot meta-analysis of regurgitation as regard pre and post fundoplication.

	preoper	ative	post opera	tive		Odds Ratio	Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI			
marano	10	13	2	13	15.1%	18.33 [2.52, 133.26]				
shedeed et al, 2021	32	40	10	40	65.3%	12.00 [4.18, 34.45]				
wang et al, 2015	38	43	5	40	19.7%	53.20 [14.18, 199.53]				
Total (95% CI)		96		93	100.0%	21.05 [9.97, 44.47]	■II	₽•		
Total events	80		17							
Heterogeneity: Chin=	3.00, df= 2	(P = 0.2)	(2);1 ² = 33%	0			004	400		
Test for overall effect							0.01 0.1 10 Favours [experimental] Favours [control]	100		

Fig. (9): Forest plot meta-analysis of heart burn as regard pre and post fundoplication.

preoperative postoperative					Odds Ratio	Odds Ratio				
Study or Subgroup	Events	Total	Events	ents Total Weight		M.H, Fixed, 95% CI	M-H, Fixed, 95% CI			
he et al, 2019	51	51	2	50	6.3%	1998.20 [93.54, 42684.29]		<u> </u>		
wang et al, 2015	40	43	5	40	93.7%	93.33 [20.79, 418.93]		-		
Total (95% CI)		94		90	100.0%	213.20 [60.92, 746.11]				
Total events	91		7							
Heterogeneity: Chin=	3.21, df= 1	(P = 0.	07);1 ² :69	9%			0.01 0.1	10 100		
Test for overall effect:	Z= 8.39 (F	0.000	001)				0.01 0.1 Favours [experimental]			

Fig. (10): Forest plot meta-analysis of the use of proton pump inhibitors pre and post operative.

Discussion

Antireflux operations are aimed at creating an effective barrier to reflux at the gastroesophageal junction and thus attempt to improve physiologic and mechanical issues involved in the pathogenesis of GERD. Ideal antireflux surgery should provide durable reflux control with no troublesome functional disorders [22].

Esophageal motility is so complicated subject, and it is hard to find a group of studies that follow the same method and give the same name of parameters. Some studies reporting data as mean \pm SD and others reporting median (range), which lead to that meta-analysis could not be performed. Also, there are two ways for esophageal manometry, the traditional old one which record the conventional line tracing and the new technique which is called high resolution manometry (HRM). Another modification was introduced to measure EGJ motility using what is called the functional lumen imaging probe (Endo FLIP) that has been applied to assess lumenal distensibility in the esophageal lumen and at EGJ, also it could measure the pressure within the esophageal lumen and EGJ but gives another reading than that of manometry.

present study will discuss the effect of Nissen fundoplication on the esophageal motility and how it could change the parameters for benefit of improving GERD. The most frequent esophageal motility disorders found in GERD patients are lower esophageal sphincter (LES) hypotonia, and it was found that Nissen fundoplication is the most effective operation in increasing that impaired lower esophageal sphincter pressure and controlling reflux [23].

This systematic review and meta-analysis is done to measure the effect of Nissen fundoplication operation on the esophageal motility. This systematic review and meta-analysis includes 7 studies that measure LESP pre and post operative and some other measures of the esophageal motility. These studies are [13-16,19-21]. The first measure to be discussed here is the lower esophageal sphincter pressure. The forest plot meta-analysis is done which provide that there is significantly increase in the post Nissen fundoplication LESP than before Nissen the operation (p-value=0.002, SMD=-1.26, 95%CI between $-2.\overline{3}8$ to -1.34). The LESP in the preoperative measures range from 9.7±4.3 to 15.2±9.4, and in the postoperative measure range from 13.8±4.7 to 24.8±6.4. These results of our study match with the results obtained by Tian et al. [24] in their meta-analysis study (which performed on Six trials) and they found that there is A significant improvement in LES pressure was achieved (post operative measures range from 10.3±2.2 to 23±6.0 mm Hg) which was ranged from 4.28±6.48 to 9.9±0.0 mm Hg in the preoperative measures, Also Du et al. [22] concluded that the result of their meta-analysis suggested that laparoscopic Nissen fundoplication was associated with a higher mean postoperative LES pressure compared to laparoscopic Toupet fundoplication.

Distensibility:

Distensibility (essentially resistance to distension), rather than pressure, is useful in assessing the function of EGI (25). It was found that normative data varied widely among studies of healthy volunteers. This is potentially due to the variability in balloon sizes and FLIP protocols used, as well as the variable definition of normal subjects. Following anti-reflux procedures, distensibility fell to the range of (.1 6 mm²/mmHg) (near to achalasia measures). This drastic drop in EGJ distensibility in GERD patients after antireflux procedures suggests that FLIP EGJ measures should not be interpreted in isolation from data on esophageal body motility, as most of these post-antireflux surgery patients do not exhibit impaired esophageal emptying to the degree of achalasia. This finding also highlights the importance of screening for esophageal motility disorders prior to fundoplication is to avoid the heightened risk of pseudo-achalasia [26].

In our study there are only two studies that use FLIP to assess the distensibility of EGJ in the period of our search, these studies are de Haan et al. [17]; Turner et al. [20]. Also Chen et al. [26] had in their systematic review small number of studies using FLIP to assess distensibility of the esophagus in a heterogeneous population of subjects. Interpretation of distensibility was also made difficult due to the likelihood of non-normally distributed data, as evident by standard deviation larger than mean in several of the studies. Also studies that does not reporting data as mean \pm SD are excluded from the meta-analysis as this make meta-analysis impossible to be performed.

EndoFLIP assessment always in the operating room both prior to and following the construction of the fundoplication. FLIP parameters reported (CSA, distensibility, distensibility index). FLIP provides valuable information regarding esophageal wall compliance and lower esophageal sphincter competency that complement other diagnostic tools such as esophageal manometry and barium esophagram. Assessment of treatment adequacy intra-operatively was through intra-operative FLIP measurement (CSA and distensibility). FLIP may especially have a role in assessment of treatment response in GERD patients undergoing intervention [26].

The forest plot meta-analysis shows a significant difference between distensibility of the EGJ before and after fundoplication as the maximum value before fundoplication was 7 7mm while it became 6.3 after fundoplication (p-value <0.0001, SMDIS 0.68, 95% CI between 0.40 to 0.97) and there is no heterogeneity in the data collected. Also, on meas-

uring of the cross section area (CSA) at the EGJ pre and post fundoplication. forest plot meta-analysis found that there is significant difference between the cross-section area of the EGJ, as it is significantly decrease in post fundoplication which means successful fundoplication that permit less refluxate through the EGJ (p-value <0.0001, CI between 8.70 to 19.05, MD is 13.87 with zero heterogeneity).

Distensibility index (DI) can be calculated by dividing the cross-section area of the EGJ (CSA) by the intra-bag pressure at the EGJ. The mean minimum CSA and intra-bag pressure were calculated over a 20-s interval for each measurement and used for determining DI. The decrease of the distentibility index means more tight fundoplication that controlling reflux On performing meta-analysis forest plot for studies which record distensibility index [17,20] it was found that the distensibility index decreased significantly after Nissen fundoplication than that before fundoplication (with p-value <0.0001, MD=2.37, 95% CI between 1.71 to 3.04) which mean that Nissen fundoplication significant control on the reflux of gastric content.

In the present study distensibility index was in the preoperative measure range from 3.4 ± 3.4 to 4.6 ± 3.9 while in the postoperative results becomes 1.4 ± 0.8 which is similar to the results obtained by Chen et al. [26], in their systematic review and meta-analysis which includes 5 studies have FLIP measurements of EGI distensibility for patients with GERD; They found that following Nissen fundoplication, there is a reduction in distensibility. Prior to treatment, the measures of distensibility ranged from 2.4 to 8 mm²/mmHg at 30-40 mL bag volume. This dropped to 0.97-1 6 mm²/mmHg after fundoplication. However, future studies in larger number normal subjects and patients using standardized FLIP protocol and balloon size are needed for reliable interpretation of FLIP data.

Secondary outcomes:

Dysphagia:

Post-fundoplication dysphagia rates at 3 months range from 10 to 40% with long-term rates of up to 10% at 1 year [27]. The clinical implications of dysphagia following anti-reflux surgery have extensive effects on quality-of-life outcomes, often resulting in significant weight loss, malnutrition, reoperation rates of 1.8-10.8%, and endoscopic dilatation rates of 0-25% [28].

In our study, there is insignificant decrease in percentage of dysphagia in the postoperative period. In that present study only 3 studies that recorded preoperative and postoperative incidence of dysphagia. The preoperative percentage of dysphagia was 29.6% which was decreased to 19.7% in the post operative follow up period. Also, still dysphagia has high postoperative percentage (19.6%), this may be due several causes as post operative oede-

ma in wrap and this type of dysphagia resolve after some weeks of the operation. Another cause of postoperative dysphagia is tight wrap which could be treated either by endoscopic dilatation or redo of the operation changing it into Toupet 270° fundoplication. For this reason, most surgeons doing Nissen fundoplication use bogie (about 52-56 french) to avoid tight warping of the fundus around the lower esophagus. In the present meta-analysis 7 of the included studies used bougie during fundoplication to avoid postoperative stenosis.

Also, Du et al., [22] concluded that the small but significant incidence of dysphagia and gas-bloating syndrome associated with LNF has promoted the development of alternative strategies for the treatment of GERD (e.g., posterior and anterior partial fundoplication). However, no trials have demonstrated a significant reduction in postoperative dysphagia rate or provided clear evidence to support routine application of LTF [22].

De meesters score:

It is a composite score of the acid exposure during a prolonged ambulatory PH monitoring, it is used to categorize patients as GERD+ OR GERD- and it is estimated that the value below 14.7 is considered negative for GERD. In this meta-analysis only two studies that record their de meesters score [13, 21]. The forest plot of this meta-analysis shows that de meesters score decreased significantly post fundoplication than that it was in the pre-fundoplication period. The recorded de meesters scores in our study was in the preoperative period range from 35.22 ± 11.74 to 43 ± 42.1 to be in the postoperative period ranging from 5.55 ± 2.08 to 10.37 ± 3.1 .

Also, Du et al. [22] found in their meta-analysis on six studies that DeMeester scores was decreased after fundoplication and the postoperative reading range from 5.95±0 to 14±5. The same result obtained by Tian et al. [24] reported that the DeMeester score which is recorded by three trials was lower after LNF than that of the preoperative values. The preoperative values range from 40-2±47.6 to 181.16±92.73 in the preoperative records while in the postoperative state the demeester score significantly lower and ranging from 8.04±2.12 to 14±5.

Regurgitation and heart burn:

There are 3 studies records the effect of Nissen fundoplication on regurgitation [13,14,21]. Forest plot metanalysis of these results explains that there is significant decrease in regurgitation symptoms and heart burn symptoms after Nissen fundoplication.

In the present study the percentage of regurgitation before operation was 83.3% which turned to 10.75% post Nissen fundoplication, and the percentage of heart burn before Nissen fundoplication is 83.3% which is dropped to 18:27% in the postop-

erative period. These results agree with the results of the other meta-analysis, as Du et al. [22] in their meta-analysis study recorded postoperative percentage of regurgitation of 10.6% and the percentage of heart burn 10.4% after Nissen fundoplication which is very similar to our results. While in Tian et al. [24] meta-analysis the postoperative recurrence of GERD (heart burn and regurgitation) symptoms was higher (22.7%) than that recorded in our result, yet it is lower than those preoperative results.

Proton pump inhibitors (Ppi) use:

There only two studies which record the use of proton pump inhibitors pre- and post-fundoplication. Forest plot meta-analysis of that results shows that there is significant difference in the use of **PPI** as there significantly decreased use of **PPI** after fundoplication than before fundoplication with 96.8% use **PPI** and postoperative drops greatly to 7.7% (p-value <0.00001, ORIS 213.20., 95% CI between 60.92 to 746.11, but the heterogeneity is equal to 69%). Tian et al. **[24]** reported that only 6.69% of the patient who have Nissen fundoplication need postoperative medication of ppi due to recurrence of severe reflux symptoms in follow-up period which is very similar to our results.

Conclusion:

This meta-analysis concluded that Nissen fundoplication increase significantly the LESP which control most of the reflux symptoms as it decreases significantly the regurgitation and heart burn symptoms. Also, it found that it significantly decreases the use of proton pump inhibitors and improve life mode of the patient. But it does not significantly change the dysphagia symptoms especially in the early postoperative period. This study promote much research on the EndoFLIP manoeuvre during the operation just in the time before insufflation and after performing the wrap as this Endo FLIP assists mostly adjusting the tightness of the wrap.

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التحليل البعدى لنتيجة حركية المرىء بعد تثنية قاع نيسن

مرض الجزر المعدى المريئي (GERD) هـ و مرض منتشر للغاية. عرف مؤتمر إجماع مونتريال في عام ٢٠٠٦ ارتجاع المرىء بأنه «حالة تتطور عندما يتسبب إعادة تدفق محتويات المعدة أعراضا و / أو مضاعفات مزعجة». اعتبر مؤتمر توافق الآراء البرازيلي في عام ٢٠٠٢ أن ارتجاع المرىء هـ و «اضطراب مزمن يتعلق بالتدفق الرجعي لمحتويات المعدة والاثني عشر إلى المرىء و / أو الأعضاء المجاورة، مما يؤدي إلى مجموعة من الأعراض، مع أو بدون تلف الأنسجة». ان الفسيولوجيا المرضية لارتجاع المرىء متعددة العوامل ومعقدة، ولكنها تدور حول عدم كفاءه تقاطع المرىء المعدى (EGJ) كحاجز مضاد للارتجاع، في شكل ارتخاء العضلة العاصرة المريئية السفلية العابرة (TLESR) و / أو EGJ انخفاض للضغط في تقاطع المرىء المعدى.

تشخيص ارتجاع المرىء ليس سهلا أو مباشراً، حيث أن الأعراض غير محددة، والعرض السريري غير متجانس، وهناك تداخل كبير مع اضطرابات الجهاز الهضمي العلوي الأخرى، مثل عسر الهضم الوظيفى وخزل المعدة. يعتمد التشخيص على تقدير التشوهات الهيكلية للمرىء حيث يتكامل التنظير العلوى وابتلاع الباريوم مع التنظير العلوى للتشوهات الفسيولوجية المريئية مثل اضطراب الحركة وعدم كفاءة عضلة العاصرة المريئية السفلية باستخدام قياس ضغط المرىء، مسبار التصوير الوظيفى للتجويف. ومراقبة درجة الحموضة.

قدم نيسن جراحته الشهيرة في عام ١٩٥٦، والتي أعقبتها العديد من التعديلات الأخرى، لكن الدراسات التي استخدمت قياس الضغط التقليدى أظهرت أن تثنية القاع من نيسن كانت الأكثر فعالية في تحسين كفاءة العضلة العاصرة المريئية السفلية، وبالتالي تم تبنيها بسرعة من قبل الجراحين في أمريكا الشمالية وأوروبا، لتصبح «طريقة العمل» لمعظم الجراحين الذين يعالجون مرض الجزر المعدى المريئي (GERD) في القرن العشرين. لكن جراحة نيسن لا تزال تعانى من بعض المضاعفات مثل عسر البلع ومتلازمة لطخة الفاز، ويمكن تجنب هذه المضاعفات أثناء التشغيل باستخدام، مسبار التصوير الوظيفي للتجويف لضبط كفاءة العضلة العاصرة أو حتى استخدام البوج أثناء بناء تثنية القاع.

بعد فحص الدراسات وفقا لمعايير الإدراج والاستبعاد، وفقط الدراسات التى يتم فيها تضمين مقياس الضغط قبل الجراحة وبعدها، والتى تم العثور عليها في تسع دراسات في فترة الدراسة الحالية. شملت هذه الدراسات ١٦١ مريضاً، خضع ٣٣٧ منهم (٩٨, ٥٠٪) لعملية تثنية القاع نيسن بالمنظار (LNF)، وقاموا بإجراء قياس الضغط (إما بالطريقة التقليدية أو باستخدام مقياس ضغط عالى الدقة (HRM) قبل الجراحة وبعدها. تم نشر الدراسات المشمولة بين عامى ٢٠١٤ و٢٠٢١، مع فترة متابعة تتراوح من ٦ أشهر إلى ٥٥ شهراً.

فيما يتعلق بالوفيات، أفاد جميع المؤلفين أنه لم يكن هناك معدل وفيات في دراساتهم مما يعني أن تثنية القاع نيسن هي إجراء آمن. كما كانت الإقامة في المستشفى في غضون أسبوع واحد في المتوسط.

تهتم النتيجة الأولية بتأثير تثنية القاع نيسن على حركة المرىء وكيف يمكن أن يغير المعايير لصالح تحسين ارتجاع المرىء. حركية المرىء موضوع معقد للغاية ومن الصعب العثور على مجموعة من الدراسات التى تتبع نفس الطريقة وتعطى نفس اسماء المعايير. في هذا التحليل البعدى، سنقارن ثلاث عناصر تنتمى إلى مسبار التصوير الوظيفى للتجويف (قابلية تمدد الموصل المعدى المريئى والمساحة مقطعية في الموصل المعدى المريئي ومؤشر التمدد) ومعيار واحد تنتمى إلى مقياس الضغط التقليدى أو عالى الدقة وهو ضغط العضلة العاصرة المريئية المنخفض (LESP).