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Gastroesophageal Reflux Disease and Sleeves Gastrectomy with Different Distance to the Pyloric: A Systematic Review and Meta-Analysis

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Abstract

Objective: This systematic review and meta-analysis was performed to explore the relationship between the distance of the pyloric and Gastroesophageal Reflux Disease (GERD) after Sleeves Gastrectomy (SG).

Methods: A computerized literature search was conducted on PubMed, EMBASE, CENTRAL, and four Chinese databases for clinical studies from inception to December 2019. Data were pooled using Review Manger 5.3, and Odds Ratio (OR) with corresponding 95% Confidence Interval (95% CI) was pooled when needed. Subgroup and sensitivity analyses were performed if necessary and feasible.

Results: Twenty-three articles with a total of 4,033 patients were included. Among these studies, 12 showed an increased prevalence of GERD after SG, while 11 showed a reduced prevalence. However, the pooled result showed non-significant relation between the distance of the pyloric and GERD. Additionally, there was no significant relation between rate of the esophagitis and the distance.

Conclusion: No significant relation was found between distance of the pyloric and GERD after SG, as well as between the distance and esophagitis. But due to the high heterogeneity of the included studies, further prospectively designed studies are needed to confirm our founding.

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Introduction

Gastroesophageal Reflux Disease (GERD) is one of the tedious digestive problems, which can bring about high incidences of serious complications and make a negative impact on quality of life [1]. The symptoms of GERD include regurgitation dysphagia, laryngitis, heartburn, chronic cough and esophagitis [2]. It is showed that obesity is one of the major risk factors for GERD [3]. The prevalence of GERD in obese patients ranged from 37% to 72%, also the increasing of Body Mass Index (BMI), may caused the risk of GERD symptoms and Erosive Esophagitis (EE) increase, which was independent of demographic features and dietary intake [2].

Sleeve Gastrectomy (SG) has been proven to be a one of the importance bariatric surgery, which can provide long-term weight loss and significant improvement of obesity-related metabolic diseases [4]. At the early stage, SG was regarded as a restrictive weight-loss procedure, but a number of studies found that the mechanism involved was multi-factor, including the change of endogenous hormones level, metabolic function factor and gastric emptying factor [5]. During SG, the greater curvature of stomach needs to be destroy, with a certain distance from the pylorus. Different surgeons have different habits in this process, and various distances from the pylorus may result in different prevalence rate of GERD after surgery, but no conclusion have been drawn yet [6].

In this paper, we aimed to summary and analysis the relationship between the distance of the pyloric and GERD after laparoscopic sleeves gastrectomy.

Material and Methods

Literature search

A computerized search was conducted in PubMed, EMBASE, The Cochrane Central Register

of Controlled Trials (CENTRAL), China National Knowledge Infrastructure (CNKI), Database of Chinese Ministry of Science & Technology (Wangfang), and China Biological Medicine Database (CBM), and Database of Chinese Science and Technology Periodicals (VIP) from inception to December 2019. There were no language limitations during search. Free terms and medical subject headings were used together for literature search, including (sleeve gastrectomy and gastroesophageal reflux). The references of identified articles and reviews were also hand searched for other potential studies.

Inclusion and Exclusion criteria

Articles were eligible for inclusion if the criteria were met: publications describing pre- and post-operative prevalence of GERD and/or esophagitis in patients undergoing SG. The following exclusion criteria were used for study selection: Conference abstract, case series, articles describing SG with concomitant anti-reflux procedures, SG following previous surgical bariatric procedures, and open SG.

Primary outcome was the difference in prevalence of GERD before and after SG, assessed through GERD symptoms, or the use of anti-reflux medication, or the outcome of esophageal function tests. For articles only reported the percentage or number of patients with postoperative remission of GERD symptoms, we assessed the postoperative prevalence by preoperative percentage minus the percentage of complete remission of GERD symptoms.

Data extraction and quality assessment

Two investigators independently performed the stages of study selection, data extraction and quality assessment, and for disagreements, discussion with a third investigator would be conducted for consensus. At first, all articles would be screened to determine whether they met inclusion criteria based on titles and abstracts. And full-text would be further reviewed if necessary.

For each of enrolled studies, we would extract the following data: The first author, publication year, patients' characteristics, follow-up duration, and prevalence of GERD before and after SG, prevalence of esophagitis before and after SG, and the distance of gastrectomy from the pylorus. Regarding missing data, we would contact the authors by email for complete information if possible. We adopted the modified version of Newcastle-Ottawa scale for quality assessment; however, the item regarding "Selection of the non-exposed cohort" was removed because it was not applicable for cohort studies without a control group.

Statistical analysis

All statistical analyses were performed by Review Manager (RevMan) 5.3. Odds ratio with corresponding 95% Confidence Interval (95% CI) were calculated for continuous variables. The Cochran Q-statistic and I2 statistic was use to evaluate between-study heterogeneity. A p value <0.1 and I2>50% indicate significant heterogeneity, and then we would choose a random effect model to pool result. Otherwise, a fixed effect model would be used. Subgroup and sensitivity analyses were conducted to explore possible sources of heterogeneity if necessary and feasible. Pre-specified subgroup analyses include distance from the pylorus (2 cm to 3 cm *vs.* 4 cm to 5 cm *vs.* 6 cm *vs.* 8cm), preoperative GERD (with *vs.* without) and follow-up duration (≤ 12 months *vs.* >12 months). Sensitivity analyses were conducted by using the one-study-out method and changing the pooling models (random effects model or fixed effect model).

Results

Search process, study characteristics, and quality assessment

Database searches provided a total of 278 relevant articles and there was no other trials added by manual search. Fourteen articles were removed due to duplication, so we screened the remaining 223 articles based on titles and abstracts. Afterwards, 67 publications were identified for eligibility of inclusion criterion in full text. Then, 34 articles were included in qualitative synthesis, of which 11 had no data for quantitative synthesis. Hence, the remaining 23 articles with a total of 4033 patients were incorporated into final meta-analysis [1,5-26]. Figure 1 showed the detailed process of study selection. Table 1 presented the characteristics of included studies. These patients had different distances of pyloric from 2 cm to 8 cm, the duration of the follow-up ranged from 3 months to 120 months. Table 2 displayed the assessment of study quality.

Meta-analysis of the relationship between the distance of the pyloric and GERD

Twenty-four trials involving 4,033 patients reported the outcome of the relationship between the distance of the pyloric and GERD. Because of significant heterogeneity among these studies (P<0.00001, I2=94%), a random effects model was used to pool result, it showed that the distance of the pyloric and GERD did not have significant relationship (P=0.49, 95% CI 0.6 to 2.86) (Figure 2).

In order to explore the possible source of heterogeneity, we performed subgroup analyses by the distance of the pylorus, preoperative GERD and follow-up duration (Table 3). The distance of the pylorus have been showed a high heterogeneity result observed between 2 cm to 3 cm (P<0.00001, I2=95%), 4 cm to 5 cm (P<0.00001, I2=89%), 6 cm (P<0.0001, I2=85%), pooled result showed no significant statistics difference about the distance of the

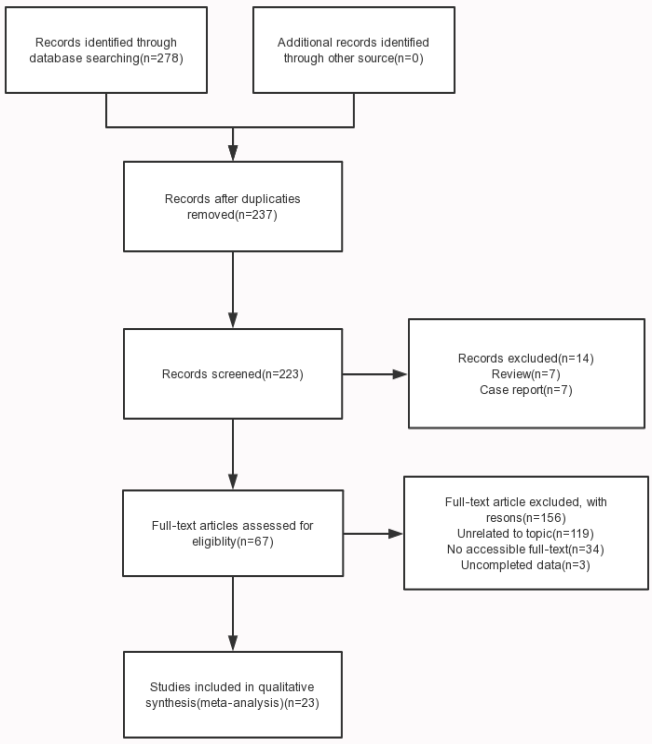

Figure 1: Flow diagram of study selection.

Table 1: Characteristic of included studies.

Study	N	Methods	GERD symptoms Pre-LSG N (%)	GERD symptoms Post-LSG N (%)	Follow-up (months)	Length begins from the pylorus (cm)
Coupaye [7]	47	manometry, 24-hour pH monitoring	6 (13)	18 (38)	12	5-6
Berry [8]	477	Symptom reporting	25 (5.24)	8 (1.68)	36	5
Kowalewski [9]	100	Symptom reporting, Medication usage	4 (4)	60 (60)	96	5-6
Viscido [10]	109	Symptom reporting, questionnaire, endoscopy medication usage	36 (33)	48 (44)	18	4-6
Georgia [11]	12	24-hour pH monitoring, and Symptom reporting	0	10 (83.3)	12	2-3
Hoyuela [1]	156	Symptom reporting	0	24 (15.3)	60	3
Genco [12]	110	Symptom reporting, manometry, 24-hour pH monitoring, endoscopy	37 (33.6)	75 (68.2)	58	6
Gadiot [13]	277	Symptom reporting, medication usage	28 (10.1)	9 (3.2)	60-96	6
Sioka [14]	18	Symptom reporting, manometry, endoscopy	18 (100)	11 (61.1)	7	5
Chuffart [15]	41	Symptom reporting	5 (12.1)	11 (26.8)	60	8
Mandeville [16]	100	Symptom reporting, Medication usage	17 (17)	44 (44)	72-120	6
Albanopoulos [17]	88	Symptom reporting	24 (27)	8 (9.2)	36	3-4
Hendricks [18]	919	Endoscopy, 24-hour pH monitoring, Symptom reporting	13 (1)	38 (4)	84	5
Seki [19]	179	Symptom reporting	0	6 (3.35)	60	4-8
Arman [20]	65	Symptom reporting, Medication usage	0	6 (9.2)	132+	5-6
Pok [21]	669	Symptom reporting	0	29 (4.3)	60	4
Sucandy [22]	131	Symptom reporting, endoscopy	67 (51.1)	35 (26.7)	18	4-6
Gorodner [23]	118	Symptom reporting, manometry, 24-hour pH monitoring	14 (11.9)	8 (6.8)	12	6
Burgerhart [24]	20	Questionnaire, manometry, 24-hour pH monitoring	14 (70)	8 (40)	3	6
Daes [26]	382	Symptom reporting, endoscopy	170 (44.5)	10 (2.6)	22	3
Sharma [25]	32	Questionnaire, endoscopy and radionuclide scintigraphy	8 (25)	4 (12.5)	12	4-5
Daes [26]	134	Symptom reporting, endoscopy	66 (49)	2 (1.5)	12	3
Howard [6]	28	Symptom reporting, endoscopy	7 (25)	11 (39)	2.5	3-4

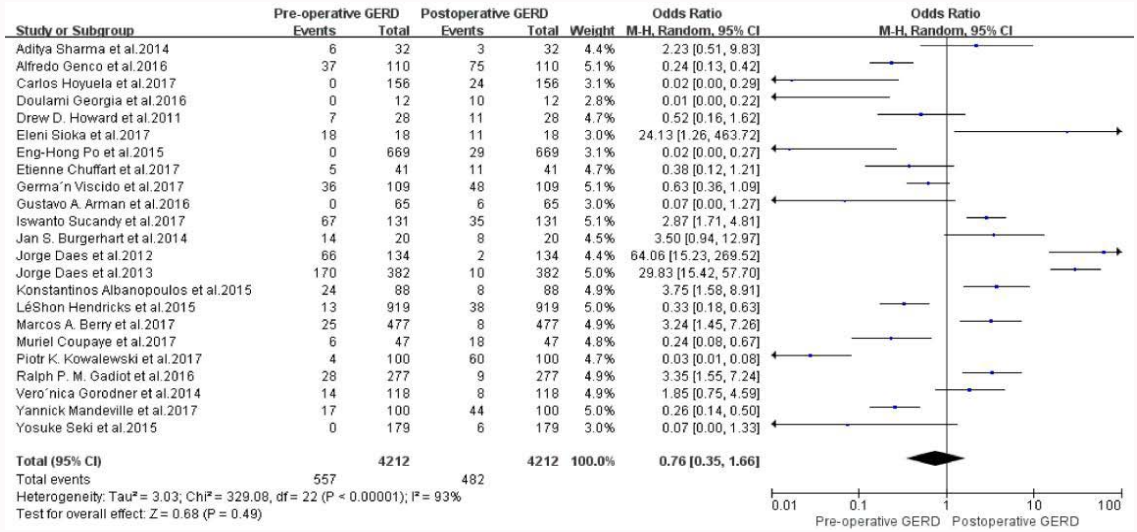

Figure 2: Forrest plot of the included studies.

pylorus (P=0.62, 0.96 and 0.21, respectively). Grouping the studies by preoperative GERD resolved the heterogeneity in the 5 studies rerolling patients without Preoperative GERD (P=0.82, I2=0%), but pooled result showed no significant difference between pre- and post-operative prevalence of GERD. Based on the follow-up duration, a significant heterogeneity result observed between short-term duration (P=0.00001, I2=88%) and long-term duration (P<0.00001, I2=94%), pooled result showed no significant difference about the duration (P=0.09 and 0.18, respectively).

In the sensitivity analysis, the effective influence of the study was confirmed by changing the random effects model to a fixed effect

Table 2: Quality assessment of included studies by modified Newcastle-Ottawa Scales.

Study	Selection			Comparability	Outcome		
	Exposed cohort	Ascertainment of exposure	Outcome of interest		Assessment of outcome	Length of follow-up	Adequacy of follow-up
Coupaye [7]	*	*	*	*	*	*	*
Berry [8]	*	*	*	*	*	*	*
Kowalewski [9]	*	*	*	*	*	-	*
Viscido [10]	*	*	*	*	*	*	*
Georgia [11]	*	*	*	*	*	*	*
Hoyuela [1]	*	*	*	*	*	*	*
Genco [12]	*	*	*	*	*	*	*
Gadiot [13]	*	*	*	*	*	-	*
Sioka [14]	*	*	*	*	*	*	*
Chuffart [15]	*		*	*	*	*	*
Mandeville [16]	*		*	*	*	*	*
Albanopoulos [17]	*	*	*	*	*	*	*
Hendricks [18]	*	*	*	*	*	*	*
Seki [19]	*	*	*	*	*	-	*
Arman [20]	*	*	*	*	*	*	*
Pok [21]	*	*	*	*	*	*	*
Sucandy [22]	*	*	*	*	*	*	*
Gorodner [23]	*	*	*	*	*	*	*
Burgerhart [24]	*	*	*	*	*	*	*
Daes [26]	*	*	*	*	*	*	*
Sharma [25]	*	*	*	*	*	*	*
Daes [26]	*	*	*	*	*	*	*
Howard [6]	*	*	*	*	*	*	*

Table 3: Subgroup analysis of preoperative GERD, and follow-up duration.

Subgroup	Stratification	No. of studies	P value for Heterogeneity	I^2	Pooled 95% CI	P value for pooled result
Distance from the pylorus	2-3 cm	4	<0.00001	95	4.79(0.01,2286.97)	0.62
	4-5 cm	4	<0.00001	89	0.96(0.19,4.96)	0.96
	6 cm	5	<0.0001	85	1.66(0.76,3.66)	0.21
	8 cm	1	-	N/A	2.64(0.83,8.45)	0.1
Preoperative GERD	With	18	<0.00001	94	0.73(0.32,1.66)	0.45
	Without	5	0.82	0	36.54(9.99,133.62)	0
Follow-up duration	≤ 12 months	7	<0.00001	88	0.37(0.09,1.58)	0.18
	>12 months	16	<0.00001	93	2.3(0.89,5.95)	0.09

model (95% CI 0.60 to 2.86, P<0.00001, I2=93%). Also, the pooled results did not markedly alter when anyone research was excluded in turn, with a range from 1.09 (95% CI 0.51 to 2.34, I2=93%) to 1.59 (95% CI 0.74 to 3.42, I2=93%).

Meta-analysis of the relationship between SG and esophagitis

Three studies examined the relationship between SG and esophagitis, with a total of 524 participants. There was significant homogeneity across these researches (P<0.00001, I2=93%), so random effect model was selected for analysis (Figure 3). The pooled result suggested that the rate of esophagitis increase after SG as compared with that before surgery (OR=26.87, 95% CI 12.6 to 57.3, P=0.13). Subgroup analysis was not performed because of limited number of included studies. To verify the robustness of polled estimate, we conduct sensitivity analysis by using different pooled models. The fixed effects model also indicated that SG could increase esophagitis in obese patients (OR=0.04, I2=93%, 95% CI 0.02 to 0.08, P<0.00001), which mean that the summary effect size is robust. No matter which study was removed, the pooled result kept statistically.

Discussion

According to the result from the meta-analysis, between-study heterogeneity was high. The incidences of GRED have been found to be increased in 12 articles, while the other 11 article indicated decreased incidence of GERD after SG. There was no conclusion can be draw yet.

Now, the mechanisms for increased or decrease prevalence of GERD after SG are still unknown, but several viewpoints had been

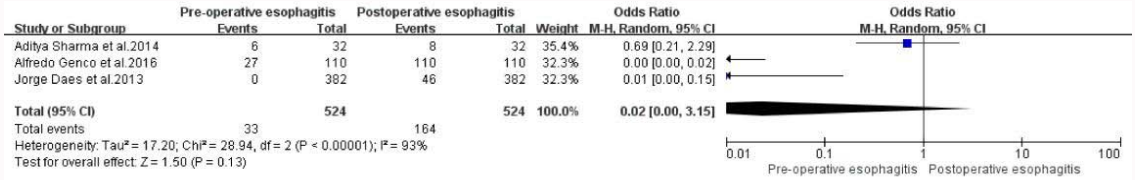

Figure 3: Forrest plot of the Meta-Analysis of the relationship between the esophagitis after SG.

issued, the anatomy structure change after the SG may caused the change of the prevalence of GERD. During the surgery, the angle of His has been destroyed, which may be increased the prevalence of GERD. Some study supported delayed gastric emptying after SG, this phenomenon can lead to increase in stomach volume and pressure, and slower motility of the gastrointestinal tract and these may be caused intragastric pressure increase [27].

Regarding the mechanisms for decreased prevalence of GERD after SG, there are also some points. Because obesity is one of the impact factor of GERD, after the surgery, the losing weight process may caused reduced the GERD, base on the change of the abdominal pressure, also the sleeve shapes of the stomach after surgery is correlated with decreased GERD [28]. And Sucandy et al. [22] discover that decreased gastric acid level to the reduction of G cell after SG could be helpful to improve GERD.

This study provides evidence about the relationship between the distance of the pylorus and GERD after SG. However, some limitations should to point out. First, it is the between-study heterogeneity; patient characteristics, follow-up duration and the distance of the pylorus vary obviously between studies and may issue in reporting biases. Nonetheless, random effects model was adopted to pool estimations when appropriate, so as to give the most conservative estimates. Furthermore, subgroup analysis and sensitivity analysis were performed and indicated that the pooled results were relatively robust. Another limitation is most of the included studies were observational studies, which are of suboptimal quality relative to experimental study. Therefore randomized controlled studies of the technique in terms of the distance of the pyloric should be performed in the future.

Conclusion

No significant relation was found between distance of the pyloric and GERD after SG, as well as between the distance and esophagitis. But due to the high heterogeneity of the included studies, further prospectively designed studies using both standardized questionnaires and objective oesophageal function tests are needed to provide more reliable answer to this important question.

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