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REVIEW ARTICLE

Long-term outcomes following Dor, Toupet, and Nissen fundoplication: a network meta-analysis of randomized controlled trials

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Abstract

Background In the surgical management of GERD, the traditional procedure is laparoscopic total (Nissen) fundoplication. However, partial fundoplication has been advocated as providing similar reflux control while potentially minimizing dysphagia. The comparative outcomes of different approaches to fundoplication are a topic of ongoing debate and long-term outcomes remain uncertain. This study aims to compare long-term gastroesophageal reflux disease (GERD) related outcomes following different fundoplication procedures.

Methods MEDLINE, EMBASE, PubMed, and CENTRAL databases were searched up to November 2022 to identify randomized controlled trials (RCTs) comparing different types of fundoplications reporting long-term (> 5 years) outcomes. The primary outcome was incidence of dysphagia. Secondary outcomes included incidence of heartburn/reflux, regurgitation, inability to belch, abdominal bloating, reoperation, and patient satisfaction. *DataParty*, which uses Python 3.8.10 was used to perform the network meta-analysis. We evaluated the overall certainty of evidence with the GRADE framework.

Results 13 RCTs were included, with 2063 patients across Nissen (360°), Dor (anterior 180°–200°), and Toupet (posterior 270°) fundoplications. Network estimates demonstrated that Toupet had lower incidence of dysphagia compared to Nissen (OR 0.285; 95% CrI 0.06–0.958). There were no differences in dysphagia between Toupet and Dor (OR 0.473, 95% CrI 0.072–2.835) or between Dor and Nissen (OR 1.689, 95% CrI 0.403–7.699). The three fundoplication types were comparable in all other outcomes.

Conclusions All three approaches of fundoplication share similar long-term outcomes, with the Toupet fundoplication likely providing the best long-term durability with lowest odds of developing postoperative dysphagia.

Keywords Fundoplication · Nissen · Toupet · Dor · Network meta-analysis · Long term

Gastroesophageal reflux disease (GERD) is a chronic digestive disorder in which a weakened lower esophageal sphincter (LES) permits retrograde flow of gastric acid into the esophagus [1]. GERD affects 18%–28% of North Americans and 10%–20% of the Western population, resulting in high costs to health care systems [2]. Pharmacological therapy via proton pump inhibitors (PPIs) represents the standard initial treatment for GERD [3]. However, past studies have found that PPIs fail to adequately relieve symptoms in up to 40% of patients [4–7]. Furthermore, multiple observational studies have correlated chronic PPI use with adverse effects such as dementia, osteoporosis, pneumonia, and increased risk of serious enteric infections inherent in acid-suppressive therapy [2].

For patients who do not respond well to PPIs, an effective alternative is anti-reflux surgery, where the gastric fundus is wrapped around the LES to mechanically increase its integrity to minimize reflux [6, 8]. Laparoscopic fundoplication is currently considered the gold standard surgical therapy for GERD [9]. Several variations are commonly performed,

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including the 360° total (Nissen), 180°–200° partial anterior (Dor), or 270° partial posterior (Toupet) wraps [10]. Ideally, anti-reflux surgery aims to resolve GERD symptoms with as few postoperative side effects as possible. While Nissen has proven effective in providing a strong anti-reflux barrier, it is also commonly associated with a higher incidence of dysphagia and gas-bloat symptoms such as bloating, abdominal discomfort, and inability to belch [11]. As such, partial fundoplication has been advocated to circumvent these mechanical side effects. However, doubts have been raised over their efficacy in controlling reflux symptoms long-term [9]. Therefore, there is ongoing uncertainty as to which wrap type is superior in controlling GERD symptoms while minimizing post-operative complications such as dysphagia and gas-related symptoms.

Several previous meta-analyses have compared outcomes following Nissen, Toupet, and Dor fundoplications [12–14]. In general, there was no statistically significant difference in postoperative complications (e.g., dysphagia, gas-bloat) and treatment effectiveness (e.g., recurrence of reflux) between complete and partial wraps [15]. However, most of these meta-analyses included only studies with short-term (less than 3–5 years) follow-up data, resulting in a lack of synthesized data on long-term outcomes. Additionally, discrepancies exist among these short-term studies, where some studies demonstrate similar reflux control between total and partial wraps and fewer side effects after partial wraps, while other studies found that total wraps had more effective reflux control in the long-term, with similar incidence of side effects compared to partial wraps [16–18]. Although a network meta-analysis (NMA) published in 2020 comparing various types of wraps concluded that Toupet fundoplication was most effective in balancing reflux symptoms and side effects including dysphagia, this was limited to mostly short-term randomized controlled trials (RCTs) and conclusions on long-term efficacy could not be made [19]. Additionally, since its publication, more long-term RCTs have published data on this topic [18, 20]. All this considered, the aim of the current systematic review and NMA was to compare patient-relevant GERD outcomes following Dor, Toupet, and Nissen fundoplication from RCTs with long-term follow-up.

Methods

Eligibility criteria

The inclusion criteria were (i) RCTs comparing two or all of the surgical interventions of interest (i.e., Nissen, Dor, Toupet fundoplications); (ii) studies which reported GERD-related adverse outcomes (e.g., dysphagia, heartburn, abdominal bloating, regurgitation, inability to belch, reoperation); (iii) studies which reported data at long-term follow-up (60 months or greater). Studies that did not specify a minimum follow-up of 60 months for reported outcomes were included if the mean follow-up time for patients was greater or equal to 60 months. Additionally, if studies reported outcomes at short-term (less than 60 months) and long-term follow-ups (60 months or greater), only the long-term data was collected. Furthermore, if multiple studies followed the same patient population, the study with the longest follow-up was selected.

The exclusion criteria were (i) participants are non-human/animal or cadavers; (ii) not a full-text article (e.g. abstract); (iii) full-text irretrievable; (iv) non-English language article; (v) RCTs with a pediatric patient population (less than 18 years of age). This review was not preregistered in an independent, institutional registry.

Outcomes assessed

The primary outcome assessed was incidence of post-operative dysphagia (solid or liquid). Postoperative dysphagia was defined as patient self-reported difficulty with swallowing. Secondary outcomes were (1) incidence of postoperative heartburn/reflux (2) incidence of postoperative regurgitation (3) inability to belch (4) incidence of abdominal bloating (5) incidence of reoperation (6) patient satisfaction with surgery. All outcomes were analyzed based on long-term follow-up data and the median (range) follow-up was reported for each outcome.

Searching and screening

Co-authors developed the search strategies and conducted searches on MEDLINE, EMBASE, PubMed and CENTRAL on January 6th, 2022, and performed an updated search on November 1st, 2022. Three separate searches were conducted on each database to identify articles comparing: (i) Nissen and Dor; (ii) Nissen and Toupet; and (iii) Toupet and Dor. The keywords and indexed headings used in each search related to the surgical procedures of interest (Nissen, Dor, or Toupet fundoplication) and GERD-related adverse outcomes (Appendix 1, 2, 3). All titles and abstracts were screened independently and in duplicate by co-authors and then compared. All authors met to resolve any discrepancies through discussion. An identical process was followed for full-text screening of eligible articles.

Data extraction

Data extraction was conducted by two reviewers on a standardized spreadsheet created a priori. Reviewers were not blinded to authors, institutions, or the journal where the manuscript was published. The following data were extracted from eligible studies: study characteristics (author,

country, year of publication, single or multi-center design, funding source, inclusion and exclusion criteria), patient demographics (number of patients included in each surgical arm, mean age at time of enrollment, % female), follow-up time points, operative characteristics [crural repair performed, bougie used, fixation of fundoplication, wrap length], GERD surgery-related adverse outcomes (incidence of postoperative dysphagia, postoperative heartburn/reflux, postoperative regurgitation, inability to belch, abdominal bloating), incidence of reoperation, and post-operative patient satisfaction.

Assessment of risk of bias and certainty of evidence

Risk of bias was assessed using the Cochrane Collaboration's tool for assessing risk of bias in RCTs [21]. The following domains were assessed: (1) random sequence generation, (2) allocation concealment, (3) blinding of study participants, personnel, and outcome assessors, and (4) incomplete outcome data (≥ 20% missing data will be considered at high risk of bias) (5) performance bias. The direct, indirect, and network meta-analysis estimates were assessed for certainty of evidence by grading of recommendations, assessment, development, and evaluation (GRADE) [22–24]. Based on risk of bias, directness, consistency, precision, evidence of publication bias, and transitivity of indirect comparisons, we rated the evidence for each outcome as high, moderate, low, or very low quality.

Data synthesis and analysis

An NMA was performed with *DataParty*, which uses Python 3.8.10 for data analysis with the following packages: Matplotlib (3.4.1), NumPy (1.20.2), Pandas (1.2.3), and SciPy (1.5.2). The preferred reporting items for systematic reviews and meta-analyses (PRISMA) extension statement for NMAs was followed for the reporting of the NMA [25]. We calculated direct, indirect, and network estimates for each treatment comparison using a random effects model and reported the combined odds ratio and 95% credible intervals (CrI). Credible intervals were used numerically to judge for statistical significance, such that if both sides of the CrI were on the same side of the null value 1.0, then the outcome was considered significant. We used vague, non-informative prior distributions, and generated the posterior distribution with four chains of 2000 samples per chain and a seed of 77. Interventions for each outcome were ranked based on the surface under the cumulative ranking curve (SUCRA) method, with values ranging from 0 to 100% which represent the probability of a given intervention being the best. We examined the node-splitting analyses produced on *DataParty* to evaluate the consistency between direct and indirect estimates for each outcome. Further, we used *RevMan 5.4* to assess heterogeneity of direct estimates using the global I^2 statistic. Additionally, we visually assessed forest plots to compare confidence intervals**.**

Results

Study characteristics

From 1191 potentially relevant citations from the search, 13 RCTs published between 1989 and 2022 met the inclusion criteria [17, 18, 20, 26–35]. Figure 1 depicts a PRISMA flow diagram for the study selection process. Studies originated from Australia ($n = 3$), Sweden ($n = 3$), South Africa ($n = 2$), China, Lithuania, Mexico, Austria, and Germany. Eligible studies reported data on three comparisons: (1) five RCTs compared Nissen and Dor fundoplication, (2) seven RCTs examined Nissen versus Toupet, and (3) one RCT compared Nissen, Toupet, and Dor fundoplication. Most studies used a minimally invasive (laparoscopic) surgery approach ($n = 12$) and one study used an open approach. The median follow-up was 91.2 months (7.6 years) (IQR: 62.5 to 186.0 months).

There were 2063 patients in total (Nissen = 1108; Toupet = 698; Dor = 257), consisting of 929 females, 1030 males, and 104 of unreported sex. The median age was 50.0 years (IQR: 47.9 to 52.1 years). In terms of surgical characteristics, crural repair was performed in six studies, not performed in five studies, and not reported in two studies. Seven studies reported utilizing a Bougie, with sizes ranging from 50 to 56 F. Lengths of wrap ranged from 1–3 cm in 6 studies, and 4 cm in one study, measured in a total of seven studies. Further, 9 of 13 RCTs reported performing a fixation of the fundoplication wrap. A summary of individual study and patient characteristics is shown in Table 1. Extracted outcome data from all studies can be found in Supplemental Tables 1–6.

Incidence of postoperative dysphagia

Five RCTs reported data for this outcome with a median follow-up of 60 months (range: 60 to 240 months), with the GRADE certainty of evidence ranging from low to moderate. In absolute terms, for patients who received Nissen, Toupet, and Dor procedures respectively, the incidence of dysphagia was 29.4% (68/231), 5.0% (6/121), and 46.3% (25/54) (Fig. 2) (Supplemental Figs. 10 and 11). Network estimates showed a 24.4% lower incidence of dysphagia in patients who received Toupet versus Nissen (OR 0.285; 95% CrI 0.06–0.958; *low certainty*), however, no significant differences existed for Nissen versus Dor and Toupet versus Dor as seen in Table 2. Further, SUCRA values in Table 3 rank Toupet (SUCRA = 90.08%) as superior to Nissen (SUCRA = 10.26%). For all the comparisons listed above, the node-splitting analysis showed that the

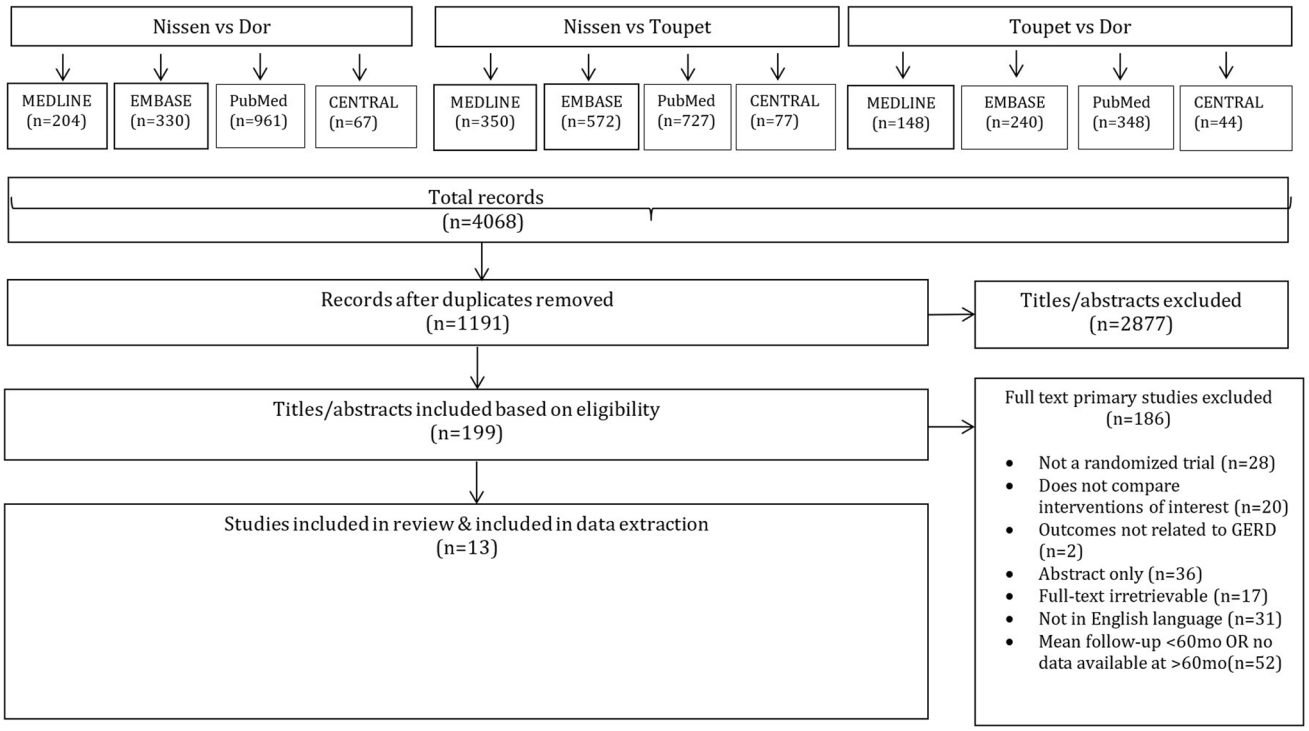

Fig. 1 PRISMA diagram

direct and indirect estimates were largely consistent with the same direction of effects.

Incidence of heartburn

Five RCTs reported data for this outcome with a median follow-up of 150 months (range: 60 to 240 months) and a low GRADE certainty of evidence for all comparisons. The incidence of heartburn for patients who received Nissen, Toupet, and Dor procedures was 30.5% (122/400), 46.1% (120/260), and 44.4% (24/54) respectively (Supplemental Figs. 1, 8, 9). However, network estimates did not reveal any significant differences for any of the three intervention group comparisons (Nissen versus Dor; Toupet versus Dor; Toupet versus Nissen) as seen in Table 2. The node-splitting analysis showed that the direct and indirect estimates were largely inconsistent for all comparisons.

Incidence of postoperative regurgitation

Three RCTs reported data for this outcome with a median follow-up of 120 months (range: 60 to 216 months), with a low GRADE certainty of evidence for all comparisons. In absolute terms, for Nissen, Toupet, and Dor procedures respectively, the incidence of postoperative regurgitation was 28.3% (36/127), 40.0% (24/60), and 43.8% (7/16) (Supplemental Figs. 2, 12, 13). However, network estimates did not reveal any significant differences for any of the three intervention group comparisons (Nissen versus Dor; Toupet versus Dor; Toupet versus Nissen) as seen in Table 2. For all the comparisons listed above, the node-splitting analysis showed that the direct and indirect estimates were largely consistent with the same direction of effects.

Re-operation required

Four RCTs reported data for this outcome with a median follow-up of 198 months (range: 144 to 216 months), with a low GRADE certainty of evidence for all comparisons. For Nissen, Toupet, and Dor procedures respectively, the incidence of re-operation was 12.7% (29/229), 5.6% (8/142), and 15.8% (12/76) (Supplemental Figs. 3, 14, 15). The types of re-operations specified include conversion of Dor fundoplication to Nissen fundoplication (n = 6), conversion of Nissen fundoplication to Dor fundoplication ($n = 5$), and revision of previous fundoplication procedures ($n = 18$ Nissen; $n = 14$ Toupet; $n = 6$ Dor). Network estimates did not reveal any significant differences for any of the two intervention group comparisons (Nissen versus Dor; Toupet versus Nissen) as seen in Table 2. For all the comparisons listed above, the node-splitting analysis showed that the direct and indirect estimates were largely consistent with the same direction of effects.

Table 1 Study and patient characteristics

Author (Year)	Country	Study design	Surgical arm	*N* Analyzed	*N* (%) Female	Mean age (SD) (Years)	Mean (SD) follow-up (months)	Crural repair performed?	Bougie used? (If yes, value in F)	Fixation of fundoplication?	Wrap length (cm)	Open or minimally invasive surgery (MIS)?
360 versus 180 degrees fundoplication												
Rudolph-Stringer et al. 2022	Australia	Double blind RCT	Nissen	41	–	–	213 (15)	No	52	No	1–2	MIS
			Dor	38	–	–	219 (15)	No	No	No	–	
Roks et al. 2017	South Africa	Double blind RCT	Nissen	52	23 (44.23)	42.5 (13.25)	143.5 (4.67)	Yes	56	Yes	–	MIS
			Dor	38	19 (50)	44.25 (13.25)	150.25 (8.5)	Yes	No	Yes	–	
Cao et al. 2012	China	Randomized trial	Nissen	47	29 (58)	59.1 (4.4)	65.3 (11.5)	Unclear	No	Yes	–	MIS
			Dor	49	34 (68)	57.2 (5.1)	64.6 (10.8)	Unclear	No	Yes	–	
Engstrom et al. 2012	Australia	Prospective randomized trial	Nissen	155	60 (38.7)	50 (18)	91.2 (56.4)	No	50–52 Fr	No	2	MIS
			Dor	107	44 (41.1)	48 (16.8)	91.2 (56.4)	No	–	No	–	
Wong et al. 2008	Australia	Single blinded RCT	Nissen	16	–	–	60 (–)	No	No	Yes	–	MIS
			Dor	9	–	–	60 (–)	No	No	Yes	–	
360 versus 270 degrees fundoplication												
Analatos et al. 2022	Sweden	Double-blind randomized clinical trial	Nissen	151	60(40)	51 (11.1)	192 (15.6)	Unclear	–	–	–	MIS
			Toupet	159	66(41)	49(11.0)	192 (15.6)	Unclear	–	–	–	
Mickevicius et al. 2013	Lithuania	Randomized trial	Nissen	60	42 (27.5)	53.7 (14.6) for 1.5 cm 49.2 (14.4) for 3 cm	60 (–)	Yes	No	Yes	1.5 or 3	MIS
			Toupet	64	37 (24.2)	52.4 (12.7) for 1.5 cm 54.8 (12.6) for 3 cm	60 (–)	Yes	No	Yes	1.5 or 3	
Mucio et al. 2012	Mexico	Prospective, single blinded RCT	Nissen	124	295 (57.6)	–	180 (–)	No	56F	Yes	2.54	MIS
				114		–	180 (–)					
				102		–	180 (–)					
			Toupet	115		–	180 (–)	No	No	Yes	–	
				109		–	180 (–)					
				103		–	180 (–)					
Mardani et al. 2011	Sweden	Prospective randomized clinical trial	Nissen	34	85 (62)	51.25 (12.25)	216 (27)	Yes	No	Yes	2–3	MIS
			Toupet	39			216 (27)	Yes	No	Yes	2–3	
Shaw et al. 2010	South Africa	Blinded randomized trial	Nissen	37	14 (37.8)	47.6 (11)	68.02 (19.98)	Yes	52 Fr	Yes	1	MIS
			Toupet	36	15 (41.7)	45.8 (10.5)	67.47 (14.81)	Yes	–	Yes	2	
Hafez et al. 2008	Austria	Randomized trial	Nissen	89	47 (35.1)	51.75 (9.5)	77.75 (20.17)	Yes	No	Yes	–	MIS
			Toupet	45		51.75 (14.25)	77.75 (30.25)	Yes	No	Yes	–	
Thor et al. 1989	Sweden	Randomized prospective trial	Nissen	12 (66.7%)	8 (50)	–	60 (–)	No	> 40 F	No	4	Open
			Toupet	19	10 (52.6)	–	60 (–)	No	–	Yes	–	

Table 1 (continued)

Author (Year)	Country	Study design	Surgical arm	*N* Analyzed	*N* (%) Female	Mean age (SD) (Years)	Mean (SD) follow-up (months)	Crural repair performed?	Bougie used? (If yes, value in F)	Fixation of fundoplication?	Wrap length (cm)	Open or minimally invasive surgery (MIS)?
360 versus 270 versus 180 degrees fundoplication studies												
Fein et al. 2008	Germany	randomized trial	Nissen	74	41 (34.2)	49 (14)	120 (–)	Yes	54 Fr	Yes	–	MIS
			Toupet	9			120 (–)	Yes	–	Yes	–	
			Dor	16			120 (–)	Yes	–	Yes	–	

RCT = randomized controlled trial

Inability to belch

Four RCTs reported data for this outcome with a median follow-up of 180 months (range: 60 to 240 months), with the GRADE certainty of evidence ranging from low to moderate. In absolute terms, for patients who received Nissen, Toupet, and Dor procedures respectively, the inability to belch was 28.7% (50/174), 15.4% (6/39), and 16% (20/125) (Supplemental Figs. 4, 16, 17). However, network estimates did not reveal any significant differences for any of the two intervention group comparisons (Nissen versus Dor; Toupet versus Nissen) as seen in Table 2. The node-splitting analysis showed that the direct and indirect estimates were inconsistent for the Nissen versus Dor comparison with different directions of effect, but consistent for the Toupet versus Nissen comparison with the same direction of effects.

Incidence of abdominal bloating

Four RCTs reported data for this outcome with a median follow-up of 180 months (range: 60 to 240 months), with a low GRADE certainty of evidence for all comparisons. In absolute terms, for Nissen, Toupet, and Dor procedures, respectively, the incidence of abdominal bloating was 50.3% (94/187), 39.8% (41/103), and 50.0% (38/76) (Supplemental Figs. 5, 18, 19). However, network estimates did not reveal any significant differences for any of the two intervention group comparisons (Nissen versus Dor; Toupet versus Nissen) as seen in Table 2. The node-splitting analysis showed that the direct and indirect estimates were inconsistent for the Nissen versus Dor comparison with different directions of effect, but consistent for the Toupet versus Nissen comparison with the same direction of effects.

Patient satisfaction

Four RCTs reported dichotomous data for this outcome with a median follow-up of 102 months (range: 60 to 240 months), with a moderate GRADE certainty of evidence for all comparisons. In these studies, patient satisfaction was classified as dichotomous yes or no answer to questions: (1) patient would opt for surgery again ($n = 2$ RCTs) and (2) patient would recommend the surgical procedures to others ($n = 2$ RCTs). In absolute terms, for patients receiving Nissen, Toupet, and Dor procedures respectively, the number of patients satisfied was 90.4% (160/177), 97.2% (35/36), and 87.2% (109/125) (Supplemental Figs. 7, 22, 23). However, network estimates did not reveal any significant differences for any of the two intervention group comparisons (Nissen versus Dor; Toupet versus Nissen) as seen in Table 2. The node-splitting analysis showed that the direct and indirect estimates were inconsistent for the Nissen versus Dor comparison with large differences in the magnitude of effect, but

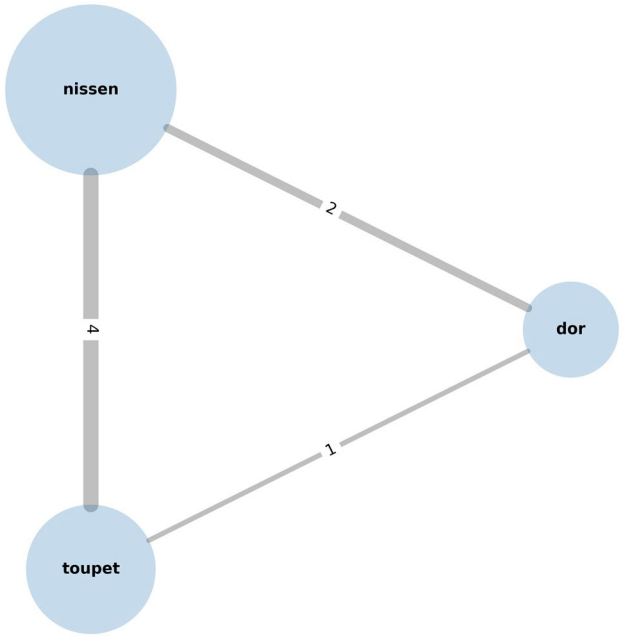

Fig. 2 Incidence of dysphagia network diagram

consistent for the Toupet versus Nissen comparison with the same direction of effects.

Risk of bias assessment

Risk of selection bias is low as all studies employed random sequence generation ($n = 13$, 100%) and most concealed allocation ($n = 11$, 85%) (Supplemental Table 7). However, blinding of participants and healthcare providers was performed in only 7 (54%) and 1 (8%) RCTs, respectively, resulting in a high risk of performance bias. Detection bias is moderate as six RCTs (46%) did not blind the outcome assessor. Complete outcome data was available in only two RCTs (15%). Since those who complete the study may not be representative of the original sample, the risk of attrition bias is rated as high. Only three (23%) RCTs published a protocol against which the reported results can be compared, thus the risk of selective reporting cannot be determined.

Assessment of certainty of evidence

The GRADE quality of evidence profile is shown in Table 2. Heterogeneity assessment of all direct estimates can be found in Supplemental Table 8. Due to moderate risk of bias, high heterogeneity, imprecise credible intervals, inconsistency between direct and indirect point estimates, and few total events (< 300 events), evidence was rated down for inconsistency, imprecision, and risk of bias. Overall, there was a low certainty of evidence for incidence of heartburn, incidence of postoperative regurgitation, incidence of reoperation, and incidence of abdominal bloating. There was low to moderate certainty of evidence for incidence of dysphagia and inability to belch. There was a moderate certainty of evidence for the number of patients satisfied.

Discussion

The current study is the first NMA comparing long-term outcomes following Nissen, Toupet, and Dor fundoplication for GERD. Low certainty evidence demonstrated the incidence of long-term dysphagia was lowest after Toupet fundoplication. However, there were no differences between

Table 2 Summary of network estimates and GRADE

	Nissen vs. Dor	Toupet vs. Dor	Toupet vs. Nissen
Incidence of heartburn	0.537 [0.018, 13.04] ⊕◯◯◯[1,2,3,]	0.701 [0.017, 23.01] ⊕◯◯◯[1,2,3,4]	1.324 [0.142, 11.58] ⊕◯◯◯[1,2,3,4,6]
Incidence of dysphagia	1.689 [0.403, 7.699] ⊕⊕◯◯[1,2]	0.473 [0.072, 2.835] ⊕◯◯◯[1,2,3]	**0.285 [0.06, 0.958]** ⊕◯◯◯[1,2]
Incidence of postoperative regurgitation	0.208 [0.012, 5.722] ⊕◯◯◯[1,2,3]	0.139 [0.004, 1.861] ⊕◯◯◯[1,2,3]	0.675 [0.031, 4.051] ⊕◯◯◯[1,2,3]
Reoperation required	0.715 [0.075, 6.394] ⊕◯◯◯[1,2,3]	N/A	0.361 [0.04, 3.777] ⊕◯◯◯[1,2.3]
Inability to belch	2.002 [0.302, 14.57] ⊕⊕◯◯[4,2]	N/A	0.32 [0.011, 11.09] ⊕◯◯◯[1,2,3]
Incidence of abdominal bloating	1.025 [0.056, 26.16] ⊕◯◯◯[2,3,5]	N/A	0.47 [0.019, 12.42] ⊕◯◯◯[1,2,3,5]
Number of patients satisfied	1.458 [0.17, 9.189] ⊕⊕◯◯[2,4]	N/A	5.743 [0.12, 579.4] ⊕⊕◯◯[2,3]

All network estimates presented as odds ratios with 95% credible intervals

GRADE rating presented from low (⊕◯◯◯) to high (⊕⊕⊕⊕)

[1]Rated down for moderate risk of bias

[2]Rated down for less than 300 events

[3]Rated down for imprecise credible interval

[4]Rated down for inconsistency between direct and indirect point estimates

[5]Rated down for moderate heterogeneity

[6]Rated down for severe heterogeneity

Table 3 Surface under the cumulative ranking curve (SUCRA) rankings

	Nissen	Toupet	Dor
Incidence of heartburn	0.6486	0.4874	0.3641
Incidence of dysphagia	0.1026	0.9008	0.4967
Incidence of postoperative regurgitation	0.5916	0.8391	0.0693
Reoperation required	0.3962	0.8887	0.2151
Inability to belch	0.1478	0.7449	0.6074
Incidence of abdominal bloating	0.3634	0.7324	0.4041
Number of patients satisfied	0.5676	0.1209	0.8115

groups in incidence of heartburn, regurgitation, bloating, or re-operation according to low certainty of evidence, and the inability to belch did not differ between comparison groups according to low to moderate certainty of evidence. Patient satisfaction also did not differ among any of the three intervention group comparisons, according to moderate certainty of evidence.

Despite decades of literature comparing different types of fundoplication, there is ongoing debate as to which surgical approach offers the best long-term outcomes. Previous pairwise meta-analyses comparing Toupet with Nissen have reported reduced incidence of dysphagia with comparable reflux control, which is in concordance with our results [1, 13, 36]. In our comparison of Dor and Nissen, no significant differences in any of the studied outcomes were identified. In contrast, previous meta-analyses of mostly short-term (< 5 years) studies have shown reduced incidence of dysphagia after Dor fundoplication, with equal reflux control and patient satisfaction compared to total fundoplication [12, 37]. Nonetheless, some authors have argued that an anterior wrap has the advantage of being technically simpler to perform compared to Nissen [38]. Further, our NMA also revealed no differences between Dor and Toupet fundoplication. Conversely, other studies have found inferior heartburn control after Dor compared to Toupet, but this is counterbalanced by less dysphagia in the early postoperative period [39, 40]. However, in the long term, differences in dysphagia between the two types of fundoplication disappeared [27, 39, 40]. Previous meta-analyses have generalized different types of wraps into one category, for instance, comparing Nissen to a "partial" group of both Dor and Toupet, or comparing Dor to a "posterior" group consisting of both Toupet and Nissen [14, 39, 41, 42]. Given the heterogeneous nature of these procedures, it is not possible to draw conclusions on the optimal anti-reflux surgery from these studies [14, 39, 41–43]. An NMA in 2018 with up to 10 years of follow-up concluded that Toupet fundoplication achieves the best balance between reflux control and dysphagia, in comparison with other anti-reflux procedures [44]. However, this study included open surgery and non-fundoplication approaches, including the obsolete Angelchik™ prosthesis, thus limiting its external validity. A 2020 NMA comparing different types of wraps similarly found that Toupet fundoplication was the most successful in managing reflux symptoms and minimizing side effects such as dysphagia. However, this NMA primarily focused on short-term RCTs (less than 5 years), which means that definitive conclusions regarding long-term effectiveness could not be drawn [19].

The present study has several implications for existing guidelines and recommendations. The most up-to-date guidelines suggest that patient preference should guide the decision on partial versus total fundoplication [8]. Patients who value reflux control over the risk of dysphagia may opt for total fundoplication, whereas in patients who wish to avoid dysphagia, partial fundoplication may be the preferred option. These guidelines do not touch on the choice between partial anterior versus partial posterior fundoplication. Whereas earlier recommendations suggest that Toupet fundoplication was superior to Dor fundoplication with regards to better reflux control without increased incidence of postoperative dysphagia [9]. Notably, initial reports suggested that patients with decreased esophageal motility are more susceptible to postoperative dysphagia, and would benefit from partial wraps [45, 46]. However, many studies have failed to demonstrate a link between motility disorders and incidence of postoperative dysphagia [9, 47–49]. On the contrary, recent multi-society consensus guidelines published in 2022 indicate that partial fundoplication may be of benefit over complete fundoplication in patients with esophageal dysmotility [50]. Our study presents evidence favouring Toupet fundoplication regarding reduced dysphagia while achieving appropriate GERD control in the long term. Results from this NMA, in addition to previous evidence of short-term advantages of Toupet fundoplication, may encourage a shift towards increasing the proportion of Toupet procedures for patients undergoing surgery for reflux. Population-based trend analyses are lacking in the current literature, and there is variability among institutions as to which procedure is most commonly performed. Some institutions have shown trends towards increasing proportion of partial fundoplications, whereas others continue to utilize Nissen most frequently [27, 28, 51–53]. This variation may be explained by a lack of clear consensus as well as regional differences in opinion and experience. Volume-outcome relationships with respect to perioperative outcomes have been reported, suggesting the existence of a learning curve associated with different fundoplication types [54–58]. Some surgeons may continue to perform the procedure for which they were trained and are most comfortable with. One could argue that this is acceptable, especially when considering most of our outcomes show equivalence between the different fundoplication types. However, even within procedure groups, variation in technique may

influence outcomes. For example, some surgeons may make the wraps very tight while others keep it loose, and some surgeons may use a bougie while others do not. A wrap sutured too tightly can lead to dysphagia, whereas one created too loose can reduce anti-reflux effectiveness as well as increase the chances of hiatal hernia [59, 60]. Ultimately, the measure of success after a surgical procedure is highly influenced by the patient's view of the outcome. If there does exist a trade-off between heartburn control and dysphagia amongst different wrap types, these seem to balance each out, as reflected in similar rates of satisfaction in the long term. The weight placed on controlling reflux, dysphagia, and other gas-related symptoms are highly individualized, which is why present guidelines recommend placing emphasis on patient preference in selecting the type of anti-reflux surgery to pursue [8].

A major strength of this study is it being the first NMA examining long-term outcomes following fundoplication for GERD. A network meta-analysis has advantages over a traditional pairwise meta-analysis as it can estimate comparative effects that have not been examined in randomized trials and draws strength from indirect evidence to gain certainty about all treatment comparisons. Furthermore, our study incorporated efforts to reduce the potential for bias using a comprehensive literature search strategy, performing quality assessment and data extraction with duplicate reviewers, and using rigorous statistical methods. However, this study does carry limitations that require consideration. First, for subjective reporting of symptoms, some studies utilized various rating scales and grading systems, whereas others used dichotomous yes/no questionnaires to the resolution of their symptoms. To err on the side of accurately comparing complete resolution or recurrence of symptoms, our analysis included only studies that clearly reported the presence or absence of symptoms. Secondly, there is evidence that obesity and weight gain are associated with poorer long-term reflux control after fundoplication [61, 62]. As the included trials did not report body mass index pre- and postoperatively, this factor could not be controlled and may represent residual confounding. Additionally, as with all NMAs, our analysis was based on the assumption that all the data were similar enough to be analyzed together [63]. Moreover, as the strength of an NMA is influenced by the amount of evidence a treatment carries and the number of comparisons made between treatments, an imbalance in the amount of available evidence may impact its power and reliability [64]. For instance, some comparisons were informed by several RCTs (e.g. seven RCTs for 360 versus 270 degrees fundoplication), whereas other comparisons were only sparsely informed (one RCT comparing 360 versus 270 versus 180 degrees fundoplication). Additionally, variability could have existed in the definitions used by studies for items such as belching, regurgitation, and abdominal bloating. Even in situations where comparisons were informed by guidelines or multiple studies, different thresholds may have been implemented, which would affect the validity of pooled data. Moreover, the variability in long-term follow-ups for many outcomes adds some nuance to our results. For example, for post-operative dysphagia, 3 RCTs had an approximate patient follow-up of 60 months [30, 33, 35], 1 RCT had a follow-up of 120 months [28], and 1 RCT had a follow-up of 180–240 months; studies with longer follow-up may hold more weight [18]. Unfortunately, due to the limited number of RCTs with long-term data, a subgroup analysis to address this variability could not be performed. Lastly, some of our outcomes display incoherence, wherein the results from the indirect comparisons largely differ from those of the direct comparisons. As such, these network estimates should be interpreted with caution, as they are based on contradicting results. Ultimately, this study illustrates the gaps in the evidence and may help orient future research towards the need for large, well-controlled trials with long-term follow-up.

Conclusion

The present review presents low certainty evidence that Toupet fundoplication may be preferable over Nissen fundoplication with respect to minimizing dysphagia, with equivalent control of GERD symptoms and other unwanted side effects. Guideline developers, healthcare institutions, and surgeons may take these results into account when making decisions about what type of fundoplication to proceed with for patients with GERD. Future well-controlled studies with standardized methods of reporting outcomes are warranted to further clarify long-term results after different fundoplication techniques.

Appendix 1

Search strategy for Nissen versus Dor comparison

1. Nissen fundoplication.mp.
2. Total fundoplication.mp.
3. Nissen.mp.
4. 360 degree fundoplication.mp.
5. 360-degree fundoplication.mp.
6. 1 or 2 or 3 or 4 or 5.
7. 180 degree partial fundoplication.mp.
8. Anterior partial fundoplication.mp.
9. Anterior fundoplication.mp.
10. Dor fundoplication.mp.
11. Partial fundoplication.mp.
12. 180-degree fundoplication.mp.
13. 180-degree partial fundoplication.mp.

14. 7 or 8 or 9 or 10 or 11 or 12 or 13.
15. Reflux.mp.
16. exp gastroesophageal reflux/.
17. (gastro-esophageal reflux disease or gastrooesophageal reflux disease or gastroesophageal reflux disease or gastrooesophageal reflux disease or gastroesophageal reflux or gastrooesophageal reflux).mp.
18. GERD.mp.
19. (anti-reflux or antireflux).mp.
20. 15 or 16 or 17 or 18 or 19.
21. 6 and 14 and 20.
22. Remove duplicates from 21.

Appendix 2

Search strategy for Nissen versus Toupet comparison

1. (Nissen Fundoplication or Total Fundoplication or Nissen or 360 Degree Fundoplication or 360-Degree Fundoplication).mp.
2. Toupet fundoplication.mp.
3. Toupet.mp.
4. 270 Degree fundoplication.mp.
5. 270-Degree fundoplication.mp.
6. 270 degree wrap.mp.
7. 270-degree wrap.mp.
8. Posterior fundoplication.mp.
9. Posterior partial fundoplication.mp.
10. 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9.
11. exp gastroesophageal reflux/
12. (Reflux or gastro-esophageal reflux disease or gastrooesophageal reflux disease or gastroesophageal reflux disease or gastrooesophageal reflux disease or gastroesophageal reflux or gastrooesophageal reflux or GERD or anti-reflux or antireflux).mp.
13. 11 or 12.
14. 1 and 10 and 13.
15. Remove duplicates from 14.

Appendix 3

Search strategy for Toupet versus Dor comparison

1. (Toupet fundoplication or Toupet or 270 degree fundoplication or 270-degree fundoplication or 270 degree wrap or 270-degree wrap or posterior fundoplication or posterior partial fundoplication).mp.
2. (180 degree partial fundoplication or anterior partial fundoplication or anterior fundoplication or Dor fundoplication or partial fundoplication or 180-degree fundoplication or 180-degree partial fundoplication).mp.
3. exp gastroesophageal reflux/.
4. (Reflux or gastro-esophageal reflux disease or gastrooesophageal reflux disease or gastroesophageal reflux disease or gastrooesophageal reflux disease or gastroesophageal reflux or gastrooesophageal reflux or GERD or anti-reflux or antireflux).mp.
5. 3 or 4.
6. 1 and 2 and 5.
7. Remove duplicates from 6.

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Declarations

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