SCIENTIFIC REVIEW



Association Between Circular Stapler Diameter and Stricture Rates Following Gastrointestinal Anastomosis: Systematic Review and Meta-analysis

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Abstract

Background Stricture is a common complication of gastrointestinal (GI) anastomoses, associated with impaired quality of life, risk of malnutrition, and further interventions. This systematic review and meta-analysis aimed to determine the association between circular stapler diameter and anastomotic stricture rates throughout the GI tract. *Methods* A systematic literature search of EMBASE, MEDLINE and Cochrane Library was performed. The primary outcome was the rate of radiologically or endoscopically confirmed anastomotic stricture. Pooled odds ratios (OR) were calculated using random-effects models to determine the effect of circular stapler diameter on stricture rates in different regions of the GI tract.

Results Twenty-one studies were identified: seven oesophageal, twelve gastric, and three lower GI. Smaller stapler sizes were strongly associated with higher anastomotic stricture rates throughout the GI tract. The oesophageal anastomosis studies showed; 21 versus 25 mm circular stapler: OR 4.39 ([95% CI 2.12, 9.07]; P < 0.0001); 25 versus 28/29 mm circular stapler: OR 1.71 ([95% CI 1.15, 2.53]; P < 0.008). Gastric studies showed; 21 versus 25 mm circular stapler: OR 3.12 ([95% CI 2.23, 4.36]; P < 0.00001); 25 versus 28/29 mm circular stapler: OR 7.67 ([95% CI 1.86, 31.57]; P < 0.005). Few lower GI studies were identified, though a similar trend was found: 25 versus 28/29 mm circular stapler: pooled OR 2.61 ([95% CI 0.82, 8.29]; P = 0.100).

Conclusions The use of larger circular stapler sizes is strongly associated with reduced risk of anastomotic stricture in the upper GI tract, though data from lower GI joins are limited.

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Introduction

Stricture is a common late complication of anastomoses in both the upper and lower gastrointestinal (GI) tract [1–3]. Anastomotic stricture has been reported to occur in 1.6–40% of patients, depending on anastomotic location, surgical technique, and other patient factors [4]. Upper GI tract strictures can be associated with dysphagia, reflux, inability to tolerate diet, and secondary complications such as pulmonary aspiration. Lower GI tract strictures can be associated with abdominal pain, bloating, constipation, and frank obstruction. Strictures all along the GI tract can result in impaired quality of life, risk of malnutrition, and the need for endoscopic or surgical intervention with risk of further complications such as anastomotic rupture [3, 5, 6].

Anastomotic stricture may occur regardless of the technique used, and previous meta-analyses have compared hand-sewn anastomosis with circular or linear stapled techniques [7–10]. The use of circular staplers has a well-established role in both upper and lower GI surgery, and numerous published studies have investigated the effect of stapler diameter on subsequent anastomotic stricture rates [11–15]. However, only one systematic review to date has synthesised these results, which looked primarily at bariatric surgery [11].

Therefore, to guide clinical practice, the aim of this systematic review and meta-analysis was to assess the impact of circular stapler diameter on anastomotic stricture rates throughout the GI tract.

Methods

A systematic review and meta-analysis were performed in accordance with the PRISMA guidelines [16] (Fig. 1). The MEDLINE, EMBASE, and Cochrane Library databases were searched from 1980 to January 2017 using the search terms "circular stapler", "anastomosis", "stapler", "size", "millimeters", "diameter", "stricture", "stenosis", and MeSH headings "surgical stapling" (MeSH), "surgical staplers" (MeSH), "surgical anastomosis" (MeSH), "pathologic constriction" (MeSH) in combination with the Boolean operators "AND" or "OR". Other articles were identified by hand-searching reference lists from retrieved articles. Identified titles and abstracts were then scrutinized by two independent reviewers (WA and CW) to determine eligibility for full-text review. Any discrepancies between the two reviewers were settled by discussion and consensus, with arbitration by a third reviewer (GOG) if necessary.

Studies investigating patients undergoing circular stapled GI anastomoses were included, regardless of the



operation or location of the anastomosis. Both randomized and non-randomized comparative studies were included, provided at least two circular stapler diameters were compared. Studies that included patients with sutured or linear stapled anastomoses were included, provided they also compared two or more circular stapler diameters. Papers available only as conference abstracts and non-English language articles were excluded. For studies investigating more than one region of the GI tract, results for each anastomotic location were analysed separately. Both cervical and thoracic anastomoses post-oesophageal resection were included. Patients undergoing either oncological or benign resections were included. The quality of observational studies was assessed using the Newcastle-Ottawa Scale [17], while the Jadad scoring system was used for randomized trials [18]. A sensitivity analysis was performed on studies scoring 5 or below in the Newcastle-Ottawa Scale to assess for inclusion into the statistical analysis.

One reviewer (WA) extracted data points from the acquired full texts and a second reviewer (CW) confirmed these. The data points extracted were: year of study, study design, number of participants, mean/median age, male/ female ratio, operation location, nature of anastomotic strictures, level of oesophageal anastomosis, follow-up period, time-to-stricture interval, stapler sizes, and stricture rates.

Statistical analysis was performed using Review Manager 5.3 (RevMan 5.3) software (Cochrane Collaboration). The primary outcome for the meta-analysis was the incidence of symptomatic GI stricture confirmed by endoscopic or radiological methods. Pooled odds ratios were calculated for different regions of the GI tract; oesophagus, gastric, and lower GI. If the oesophagus was included in any join, then it was classified as an oesophageal anastomosis. Pooled outcome measures were determined using random-effects models. A *P* value of <0.05 was considered statistically significant. Assessment of heterogeneity was also assessed through the I^2 statistic as Cochran's Q has shown to be poor at detecting true heterogeneity between studies [19]. Publication bias was also assessed by funnel plots in Review Manager 5.3.

Results

Twenty-one studies were included (Table 1), representing a total of 7226 patients [12, 13, 15, 20–37]. Seven oesophageal, twelve gastric, and three lower GI studies were identified. One study assessed data from both gastric and oesophageal surgery [13]. Only one randomized controlled trial was identified [12], with the remainder being prospective or retrospective observational studies. Strictures were associated with both benign and malignant indications for surgery (see Table 1). The primary outcomes of stricture incidence for each study are reported in Table 2. The Newcastle–Ottawa Score of each study is shown in Supplementary Table 1, with a median score of 7 (range 4–9). Outcome reporting bias and publication bias were assessed via a funnel plot (Supplementary Fig. 1).

Oesophageal anastomosis

The seven oesophageal studies encompassed 1081 patients [13, 27, 28, 32, 35–37]. For the pooled oesophageal anastomosis studies, a clear increase in stricture rates was observed with the use of smaller circular stapler diameters. Stricture rates amongst oesophageal anastomosis ranged from 3 to 100% (Table 2) with a mean of 31%. The mean stricture rate for 21 mm diameter stapled anastomoses was $72\% \pm 24$ (Standard deviation), $23\% \pm 16$ for 25 mm diameter, and $16\% \pm 17$ for 28/29 mm diameter. Comparing 21 to 25 mm showed a substantial increase in stricture rates (Fig. 2a; pooled odds ratio (OR) 4.39 ([95% CI: 2.12, 9.07]; P < 0.0001, $I^2 = 0\%$). Comparing 25 mm with 28/29 mm showed the same relationship with higher stricture rates being associated with smaller stapler sizes (Fig. 2b pooled OR 1.71 ([95% CI: 1.15, 2.53]; P = 0.008, $I^2 = 2\%$).

Gastric anastomosis

The twelve gastric studies encompassed 4331 patients [12, 13, 15, 20, 21, 24, 25, 29–31, 33, 34]. These papers similarly showed strong associations between increased stricture rates and smaller-diameter circular staplers. Stricture rates amongst gastric anastomosis ranged from 0 to 60% (Table 2) with a mean of 13%. The mean stricture rate for 21 mm diameter stapled anastomoses was $22\% \pm 15$, $10\% \pm 11$ for 25 mm diameter, and $1\% \pm 1$ for 28/29 mm diameter. Comparing 21–25 mm demonstrated a substantial increase in stricture rates with the smaller stapler (Fig. 3a; pooled OR 3.12 ([95% CI: 2.23, 4.36]; P < 0.00001, $I^2 = 13\%$. A larger effect was observed when comparing the 25 mm stapler with 28/29 mm (Fig. 3b; pooled OR 7.67 ([95% CI: 1.86, 31.57]; P = 0.005, $I^2 = 0\%$).

Lower GI anastomosis

The three lower GI studies encompassed 188 patients, all from studies involving ileal pouch-anal anastomoses [22, 23, 26]. Stricture rates amongst lower GI anastomosis ranged from 9 to 60% (Table 2) with a mean of 39%. The mean stricture rate for 25 mm diameter stapled anastomoses was $51\% \pm 13$, and $26\% \pm 15$ for 28/29 mm

Table 1 Description of the included studies

Study	Year	Type of study	Number of patients (%Female)	Region of GI tract	Surgical indication	Mean age	Anastomotic leak rate (%)
Berrisford et al. [36]	1996	Observational	124 (29)	Oesophagus	Malignant disease	63.7	3.2
Cakabay et al. [28]	2012	Observational	60 (35)	Oesophagus	Not specified	Group A-55.93	3.3
						Group B-58.43	
Deldycke et al. [32]	2016	Observational	291 (19.6)	Oesophagus	Malignant	61.7	5.6
Dresner et al. [27]	2000	Observational	222	Oesophagus	Malignant and benign disease	Not specified	3.0
Johansson et al. [13]	2000	Observational (Oesophagectomy)	107 (29)	Oesophagus	Malignant and benign disease	66	1.9
Petrin et al. [35]	2000	Observational	187 (11.8)	Oesophagus	Not specified	58.6	Not specified
Yendamuri et al. [37]	2011	Observational	90 (10)	Oesophagus	Malignant	Group A-71 Group B-50	3.3
Fisher et al. [12]	2007	RCT	200 (80)	Gastric	Morbid obesity	44	0
Gould et al. [30]	2006	Observational	226 (84)	Gastric	Not specified	44	Not specified
Johansson et al. [13]	2000	Observational (Gastrectomy)	149 (30)	Gastric	Malignant and benign disease	70	6.0
Khoraki et al. [20]	2016	Observational	876 (80)	Gastric	Morbid obesity	46.9	Not specified
Kim et al. [31]	2012	Observational	1031 (32)	Gastric	Malignant	Not specified	0
Nguyen et al. [15]	2003	Observational	185 (89)	Gastric	Morbid obesity	39	Not specified
Sima et al. [25]	2016	Observational	489 (80.2)	Gastric	Morbid obesity	38	Not specified
Smith et al. [29]	2011	Observational	261 (83)	Gastric	Morbid obesity	45	Not specified
Suggs et al. [34]	2007	Observational	438	Gastric	Morbid obesity	Not specified	1.1
Takata et al. [33]	2007	Observational	379 (84)	Gastric	Morbid obesity	45	Not specified
Tokunaga et al. [24]	1999	Observational	45 (30)	Gastric	Malignant	67	0
Zuiki et al. [21]	2013	Observational	52 (24)	Gastric	Malignant	66	1.5
Kissin et al. [23]	1985	Observational	38 (55)	Lower GI	Benign and malignant	64.2	10
Lewis et al. [26]	1994	Observational	102 (49)	Lower GI	IBD/FAP	35	Not specified
Senapati et al. [22]	1996	Observational	48 (44)	Lower GI	IBD/FAP	33.2	Not specified

diameter. The pooled comparison between 25 and 28/29 mm also showed a trend towards higher stricture rates with the smaller stapler size although this did not reach the significance threshold with the limited available data (Fig. 4; pooled OR 2.61 ([95% CI: 0.82,8.29]; P = 0.100, $I^2 = 50\%$). One paper was found that compared 28/29 with 31/33 mm (ileal pouch-anal anastomosis, 2120 patients), which showed no difference in stricture rates between the two groups (14).

Sensitivity analysis and tests for bias

A sensitivity analysis was performed, evaluating for study quality. All results reported above for gastric and oeso-phageal stricture rates remained significant when studies of Newcastle–Ottawa grade 4–5 were excluded (all P < 0.01). Funnel plots were performed to assess publication bias, demonstrating no significant bias within the limited number of available studies (Supplementary Fig. 1).

Table 2	Data	from	the	included	studies

Study	Number of	Region of GI	Follow-up	Mean time-to-stricture	Stricture rates*		
	patients	tract	(years)	interval	21 mm	25 mm	28/29 mm
Berrisford et al. [36]	124	Oesophagus	4	30 weeks	4/9 (44%)	16/75 (21%)	2/37 (5%)
Cakabay et al. [28]	60	Oesophagus	Not specified	Not specified	-	1/30 (3%)	1/30 (3%)
Deldycke et al. [32]	291	Oesophagus	>5	Not specified	3/3 (100%)	25/121 (21%)	19/166 (11%)
Dresner et al. [27]	222	Oesophagus	Not specified	13 weeks	8/10 (80%)	25/78 (32%)	19/81 (23%)
Johansson et al. [13]	107	Oesophagus	5	12 weeks	-	16/30 (53%)	13/25 (52%)
Petrin et al. [35]	187	Oesophagus	3	18 weeks	5/8 (63%)	14/84 (17%)	4/93 (4%)
Yendamuri et al. [37]	90	Oesophagus	10	Not specified	-	3/24 (13%)	10/65 (15%)
Fisher et al. [12]	200	Gastric	1.5	Group A-4.8 weeks Group B-8.9 weeks	17/100 (17%)	7/100 (7%)	-
Gould et al. [30]	226	Gastric	1	12.2 weeks	23/145 (16%)	5/81 (6%)	_
Johansson et al. [13]	149	Gastric	5	Not specified	-	6/57 (11%)	1/51 (2%)
Khoraki et al. [20]	876	Gastric	1	8 weeks	20/153 (13%)	56/717 (8%)	
Kim et al. [31]	1031	Gastric	1	Not specified	_	2/384 (1%)	1/647 (0%)
Nguyen et al. [15]	185	Gastric	Not specified	7 weeks	19/71 (27%)	10/114 (9%)	-
Sima et al. [25]	489	Gastric	5	Not specified	11/88 (13%)	7/298 (2%)	_
Smith et al. [29]	261	Gastric	5	Not specified	23/145 (16%)	7/116 (6%)	_
Suggs et al. [34]	438	Gastric	4	Group A-76.9 weeks	6/64 (9%)	11/374 (3%)	_
				Group B-63.7 weeks			
Takata et al. [33]	379	Gastric	2	30.7 weeks	3/13 (23%)	4/154 (3%)	-
Tokunaga et al. [24]	45	Gastric	1	Not specified	-	5/12 (42%)	0/31 (0%)
Zuiki et al. [21]	52	Gastric	3	Not specified	3/5 (60%)	8/47 (17%)	
Kissin et al. [23]	38	Lower GI	2	Not specified	_	3/5 (60%)	2/23 (9%)
Lewis et al. [26]	102	Lower GI	3	Not specified	_	13/23 (57%)	20/59 (34%)
Senapati et al.	48	Lower GI	Not specified	Not specified	-	7/19 (37%)	7/20 (35%)

*Stricture rates are expressed as number of strictures/number of patients, for each stapler size

Discussion

This systematic review and meta-analysis investigated the impact of circular stapler diameter on anastomotic stricture rates in the GI tract. A strong correlation was demonstrated between smaller stapler diameters and higher stricture rates, particularly in oesophageal and gastric anastomoses. A nonsignificant trend was found in lower GI anastomoses amongst the few studies identified from this region.

A previous meta-analysis of patients undergoing bariatric surgery also identified that smaller stapler diameters were associated with higher anastomotic stricture rates [11]. This study expands on those results by including seven additional gastric studies (2903 additional patients) as well as including data from all other regions of the GI tract. Only one randomized trial has compared circular stapler diameters in GI surgery [12]. In that study, Fischer et al. [12] identified anastomoses with a 21-mm stapler was associated with a doubled stricture rate compared with a 25-mm stapler in patients undergoing Roux-en-Y gastric bypass. More generally, our results also show that rates of

(a)	21m	m	25m	m		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
Berrisford et al.	4	9	16	75	25.9%	2.95 [0.71, 12.28]	· · · · · · · · · · · · · · · · · · ·
Deldycke et al.	3	3	25	121	5.9%	26.49 [1.33, 529.50]	│ — — →
Dresner et al.	8	25	10	78	46.0%	3.20 [1.10, 9.34]	
Petrin et al.	5	8	14	84	22.2%	8.33 [1.78, 38.95]	│
Total (95% CI)		45		358	100.0%	4.39 [2.12, 9.07]	
Total events	20		65				
Heterogeneity: Tau ² = Test for overall effect:	= 0.00; Ch : Z = 3.99	ni² = 2) (P < 1	.70, df = 0.0001)	3 (P =	0.44); I ² =	= 0%	0.01 0.1 1 10 100 Favours [21mm] Favours [25mm]
(b)	25mm	ı	28/29m	ım		Odds Ratio	Odds Ratio
Churcher and Carls and areas							
Study or Subgroup	Events	Total	Events [·]	Total	Weight M	1-H, Random, 95% Cl	M-H, Random, 95% Cl
Cakabay et al.	Events 1	Total 30	Events 1	Total 30	Weight M 1.9%	1-H, Random, 95% Cl 1.00 [0.06, 16.76]	M-H, Random, 95% CI
Cakabay et al. Deldycke et al.	Events 1 25	Total 30 121	Events	Total 30 166	Weight M 1.9% 34.9%	1-H, Random, 95% CI 1.00 [0.06, 16.76] 2.01 [1.05, 3.86]	M-H, Random, 95% Cl
Cakabay et al. Deldycke et al. Dresner et al.	Events 1 25 25	Total 30 121 78	Events 7 1 19 19	Total 30 166 81	Weight M 1.9% 34.9% 30.2% 30.2%	1-H, Random, 95% Cl 1.00 [0.06, 16.76] 2.01 [1.05, 3.86] 1.54 [0.76, 3.10]	M-H, Random, 95% Cl
Cakabay et al. Deldycke et al. Dresner et al. Johansson et al.	Events 1 25 25 16	Total 30 121 78 30	Events 1 19 19 13	Total 30 166 81 25	Weight M 1.9% 34.9% 30.2% 13.5%	1-H, Random, 95% Cl 1.00 [0.06, 16.76] 2.01 [1.05, 3.86] 1.54 [0.76, 3.10] 1.05 [0.36, 3.05]	M-H, Random, 95% Cl
Cakabay et al. Deldycke et al. Dresner et al. Johansson et al. Petrin et al.	Events 1 25 25 16 14	Total 30 121 78 30 84	Events 1 19 19 13 4	Total 30 166 81 25 93	Weight M 1.9% 34.9% 30.2% 13.5% 11.5% 11.5%	1-H, Random, 95% Cl 1.00 [0.06, 16.76] 2.01 [1.05, 3.86] 1.54 [0.76, 3.10] 1.05 [0.36, 3.05] 4.45 [1.40, 14.12]	M-H, Random, 95% Cl
Cakabay et al. Deldycke et al. Dresner et al. Johansson et al. Petrin et al. Yendamuri et al.	Events 1 25 25 16 14 3	Total 30 121 78 30 84 24	Events 1 19 19 13 4 10	Total 30 166 81 25 93 65	Weight M 1.9% 34.9% 30.2% 13.5% 11.5% 8.0%	1-H, Random, 95% Cl 1.00 [0.06, 16.76] 2.01 [1.05, 3.86] 1.54 [0.76, 3.10] 1.05 [0.36, 3.05] 4.45 [1.40, 14.12] 0.79 [0.20, 3.14]	M-H, Random, 95% Cl
Cakabay et al. Deldycke et al. Dresner et al. Johansson et al. Petrin et al. Yendamuri et al. Total (95% CI)	Events 1 25 25 16 14 3	Total 30 121 78 30 84 24 367	Events 1 19 19 13 4 10	Total 30 166 81 25 93 65 460	Weight M 1.9% 34.9% 30.2% 13.5% 11.5% 8.0% 100.0% 100.0%	1-H, Random, 95% Cl 1.00 [0.06, 16.76] 2.01 [1.05, 3.86] 1.54 [0.76, 3.10] 1.05 [0.36, 3.05] 4.45 [1.40, 14.12] 0.79 [0.20, 3.14] 1.71 [1.15, 2.53]	M-H, Random, 95% Cl
Cakabay et al. Deldycke et al. Dresner et al. Johansson et al. Petrin et al. Yendamuri et al. Total (95% CI) Total events	Events 1 25 25 16 14 3 84	Total 30 121 78 30 84 24 367	Events - 1 19 19 13 4 10 66	Fotal 30 166 81 25 93 65 460	Weight M 1.9% 34.9% 30.2% 13.5% 11.5% 8.0% 100.0% 100.0%	1-H, Random, 95% Cl 1.00 [0.06, 16.76] 2.01 [1.05, 3.86] 1.54 [0.76, 3.10] 1.05 [0.36, 3.05] 4.45 [1.40, 14.12] 0.79 [0.20, 3.14] 1.71 [1.15, 2.53]	M-H, Random, 95% Cl
Cakabay et al. Deldycke et al. Dresner et al. Johansson et al. Petrin et al. Yendamuri et al. Total (95% CI) Total events Heterogeneity: Tau ² =	Events 1 1 25 25 16 14 3 84 0.01; Chi	Total 30 121 78 30 84 24 367	Events	Total 30 166 81 25 93 65 460 (P = 0	Weight M 1.9% 34.9% 30.2% 13.5% 11.5% 8.0% 100.0% .40); 1 ² = .2	1-H, Random, 95% CI 1.00 [0.06, 16.76] 2.01 [1.05, 3.86] 1.54 [0.76, 3.10] 1.05 [0.36, 3.05] 4.45 [1.40, 14.12] 0.79 [0.20, 3.14] 1.71 [1.15, 2.53] 2% ⊢	M-H, Random, 95% Cl

Fig. 2 a Forest plot of oesophageal 21 versus 25 mm circular stapler stricture rates. b Forest plot of oesophageal 25 versus 28/29 mm circular stapler stricture rates

	21m	m	25m	m		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M–H, Random, 95% Cl
Fisher et al.	17	100	7	100	11.3%	2.72 [1.08, 6.89]	
Gould et al.	23	145	5	81	9.8%	2.87 [1.05, 7.86]	_
Khoraki et al.	20	153	56	717	26.3%	1.77 [1.03, 3.06]	 _
Nguyen et al.	19	71	10	114	13.6%	3.80 [1.65, 8.76]	
Sima et al.	11	88	7	298	10.3%	5.94 [2.23, 15.83]	
Smith et al.	23	145	7	116	12.3%	2.94 [1.21, 7.11]	
Suggs et al.	6	64	11	374	9.4%	3.41 [1.22, 9.59]	
Takata et al.	3	13	4	154	4.1%	11.25 [2.21, 57.31]	
Zuiki et al.	3	5	8	47	2.9%	7.31 [1.05, 51.10]	
Total (95% CI)		784		2001	100.0%	3.12 [2.23, 4.36]	•
Total events	125		115				
Heterogeneity: Tau ²	= 0.04; Cł	$ni^2 = 9$	22, df =	8 (P =	0.32); I ² =	= 13%	
Test for overall effect	+ 7 _ 6 63	(D) (
	L = 0.02	s (P < ().00001)				Favours [21mm] Favours [25mm]
(b)	ι. z = 0.03	s (P < 1).00001)				Favours [21mm] Favours [25mm]
(b)	25mn	s (P < (n	28/29n	nm		Odds Ratio	Godds Ratio
(b) Study or Subgroup	25mn Events	n <u>Total</u>	28/29n Events	nm Total	Weight	Odds Ratio N-H, Random, 95% Cl	Odds Ratio M-H, Random, 95% CI
(b) <u>Study or Subgroup</u> Johansson et al.	25mn <u>Events</u> 5	n <u>Total</u> 12	28/29n Events	nm <u>Total</u> 31	<u>Weight</u> 22.2%	Odds Ratio M-H, Random, 95% Cl 46.20 [2.29, 930.35]	Odds Ratio M-H, Random, 95% Cl
(b) <u>Study or Subgroup</u> Johansson et al. Kim et al.	25m n <u>Events</u> 5 6	n Total 12 57	28/29n Events 0 1	nm Total 31 51	Weight 22.2% 43.2%	Odds Ratio M-H, Random, 95% Cl 46.20 [2.29, 930.35] 5.88 [0.68, 50.63]	Odds Ratio M-H, Random, 95% Cl
(b) <u>Study or Subgroup</u> Johansson et al. Kim et al. Tokunaga et al.	25m n <u>Events</u> 5 6 2	n <u>Total</u> 12 57 384	28/29n Events 0 1	nm <u>Total</u> 31 51 647	Weight 1 22.2% 43.2% 34.6%	Odds Ratio M-H, Random, 95% Cl 46.20 [2.29, 930.35] 5.88 [0.68, 50.63] 3.38 [0.31, 37.42]	Odds Ratio M-H, Random, 95% Cl
(b) <u>Study or Subgroup</u> Johansson et al. Kim et al. Tokunaga et al. Total (95% CI)	25mn <u>Events</u> 5 6 2	n <u>Total</u> 12 57 384 453	28/29n Events 0 1	nm <u>Total</u> 31 51 647 729	Weight 1 22.2% 43.2% 34.6% 100.0%	Odds Ratio M-H, Random, 95% Cl 46.20 [2.29, 930.35] 5.88 [0.68, 50.63] 3.38 [0.31, 37.42] 7.67 [1.86, 31.57]	Odds Ratio M-H, Random, 95% CI
(b) <u>Study or Subgroup</u> Johansson et al. Kim et al. Tokunaga et al. Total (95% CI) Total events	25mn <u>Events</u> 5 6 2 13	n Total 12 57 384 453	28/29n Events 0 1 1	nm <u>Total</u> 31 51 647 729	Weight 1 22.2% 43.2% 34.6% 100.0%	Odds Ratio M-H, Random, 95% Cl 46.20 [2.29, 930.35] 5.88 [0.68, 50.63] 3.38 [0.31, 37.42] 7.67 [1.86, 31.57]	Odds Ratio M-H, Random, 95% CI
(b) <u>Study or Subgroup</u> Johansson et al. Kim et al. Tokunaga et al. Total (95% Cl) Total events Heterogeneity: Tau ² =	25mn <u>Events</u> 5 6 2 13 = 0.00; Ch	n Total 12 57 384 453 $i^2 = 1.9$	28/29n <u>Events</u> 0 1 1 2 2 00, df = 3	nm <u>Total</u> 31 51 647 729 2 (P = 0	Weight I 22.2% 43.2% 34.6% 100.0% 0.39); I ² = 12	Odds Ratio M-H, Random, 95% Cl 46.20 [2.29, 930.35] 5.88 [0.68, 50.63] 3.38 [0.31, 37.42] 7.67 [1.86, 31.57] 0%	Odds Ratio M-H, Random, 95% CI

Fig. 3 a Forest plot of gastric 21 versus 25 mm circular stapler stricture rates. b Forest plot of gastric 25 versus 28/9 mm circular stapler stricture rates



anastomotic stricture remain clinically important [4, 5, 38–41].

Multiple other factors have been implicated in anastomotic stricture including complications (e.g. ischaemia, postoperative anastomotic leakage), anastomotic location, radiotherapy, and other patient factors. Unfortunately, we found that many of these issues are inconsistently reported in the literature, preventing a reliable estimation of their relative importance. In addition, the majority of studies investigating anastomotic stricture have been observational, and therefore the potential confounding effects of these variables could not be reliably accounted for in our meta-analysis. However, the significant association identified between stapler diameter and stricture rates in this review supports a robust direct causal relationship, which may help to guide stapler selection in surgical practice.

The findings of this meta-analysis show that although smaller stapler sizes may be chosen for ease of luminal insertion in GI surgery, the associated increased rate of anastomotic stricture risks higher overall morbidity. The occurrence of strictures is associated with impaired patient quality of life, nutritional impairment, further intervention and increased healthcare expenditure [3, 5, 6]. A judgement must be made by the surgeon as to whether a larger-diameter stapler can be safely passed through the gut lumen without trauma or tearing of tissues. Data on leak rates and stapler size were limited, and it was not possible to metaanalyse this information.

The main limitation of this review is reflected in the design of included studies. Almost all included studies were observational, and therefore the effects of potential confounding variables cannot be excluded. Most identified evidence was rated as poor to moderate according the Newcastle–Ottawa Scale, with only one randomized trial included in the analysis. Few studies from lower GI surgery were identified, with pooled data showing suggestive trends that did not reach statistical significance. Further colorectal studies are clearly required to provide firm guidance about optimal stapler sizes in this region. Furthermore, the clinical implications of this study may be limited in modern laparoscopic bariatric procedures, which frequently employ sutured anastomoses with larger anastomotic diameters than those provided by circular staplers [42]. A previous systematic review demonstrated higher stricture rates following stapled oesophageal anastomoses when compared with hand-sewn [43], and the optimal anastomotic technique for each region of the GI tract remains unclear.

In conclusion, this review has identified a strong association between circular stapler diameter and stricture rates following oesophageal and gastric anastomoses. A nonsignificant trend was found for lower GI anastomoses, though available evidence was limited. In order to reduce anastomotic stricture rates throughout the GI tract, surgeons should use the largest of the circular stapler sizes analysed in this study whenever possible, as balanced against the safety of inserting the device through the confined channel of the GI lumen. Surgeons should be encouraged to customize their circular stapler size choice to the anatomy of each patient, rather than always using a constant size in their practice. Finally, novel circular stapler designs with an elliptical angled interface warrant further investigation as such designs could theoretically increase the anastomotic surface area without making luminal stapler insertion more difficult, though would increase the technical complexity of stapler design [44, 45].

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