



Comparison of anastomotic leakage rate and reoperation rate between transanal tube placement and defunctioning stoma after anterior resection: A network meta-analysis of clinical data



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ABSTRACT

Objective: Defunctioning stoma (DS) and transanal tube (TT) placement have all been reported to be effective procedures to prevent anastomotic leakage after anterior resection. However, there are few studies that directly compare the 2 procedures, and those that do are unclear.

Methods: We performed a systematic literature search from the databases of Pubmed, Embase and Cochrane library. We limited the publication date from 2008/01/01 to 2018/07/29. The bias risk of eligible randomized controlled trials and cohort studies were assessed by Cochrane Collaboration's tool and Newcastle-Ottawa Scale, respectively. The direct meta-analysis was performed by RevMan 5.3 software. The network graph, inconsistency test and comparison-adjusted funnel plot were performed by the Stata 14.0 software. The indirect meta-analysis and rank probabilities were performed by GeMTC R package.

Results: 6 randomized controlled trials and 26 cohort studies were included in our meta-analysis. All eligible studies were assessed as low risk of bias. The anastomotic leakage rate and reoperation rate was lower in the patients receiving DS or TT placement than patients with non-protection. DS shared similar anastomotic leakage rate with TT. However, the reoperation rate was significantly lower in patients receiving DS than patients receiving TT.

Conclusion: Both TT and DS were protective factors for anastomotic leakage after anterior resection for rectal cancer. DS reduced severity of anastomotic leakage in a more effective way than TT placement. However, we still suggested the routing use of TT for decreasing the risk of anastomotic leakage in anterior resection because it was cheaper and technically simpler.

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1. Introduction

In recent years, with the improvement of surgical instruments, neoadjuvant therapy, surgical skills and anatomy, an increasing rate of rectal cancer patients received sphincter-preserving surgery after anterior resection for rectal cancer [1]. However, anastomotic leakage remains one of the most feared complications of sphincter-preserving surgery after anterior resection for rectal cancer, with an incidence rate of about 10% [2–4]. Previous studies have reported that anastomotic leakage was related to higher mortality, longer hospital stay, a greater hospitalization costs and even worse

oncological outcomes [5]. Various strategies were used to prevent anastomotic leakage after anterior resection for rectal cancer, among which defunctioning stoma (DS) was the most common procedure. DS can decrease the intraluminal pressure of the anastomotic site by bypassing the bowel content, which is the most accepted mechanism of DS. However, variable disadvantages exist, such as: stoma-related morbidity and mortality, requirement for reoperation, longer hospital stay, greater hospitalization costs, inconvenience and permanent stoma [6,7]. Recently, transanal tube (TT) placement became a newly emerged procedure that prevented anastomotic leakage after anterior resection for rectal cancer [8]. Many clinical trials, meta-analyses and observational studies reported the favourable effectiveness for preventing anastomotic leakage of TT placement compared with non-protection (NP) patients [9–11]. Many studies also proved favourable outcomes of DS

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compared with NP [12,13]. However, a direct comparison between TT and DS was rarely presented. To our best of knowledge, only one study directly compared the anastomotic leakage rate and reoperation rate between TT and DS, and their results achieved no statistical significance because of the small sample size [14]. Considering this point, we performed a network meta-analysis comparing the anastomotic leakage rate and reoperation rate between TT and DS with the aim of trying to discover an alternative procedure for DS.

Materials and methods

Search strategy

We performed a systematic literature search from the database of Pubmed, Embase and Cochrane library. The search strategy was made according to various combinations of the following key words and word variants: 'transanal tube', 'rectal tube', 'rectal cancer', 'anterior resection', 'total mesorectal excision', 'TME', 'anastomotic failure', 'anastomotic leak', 'stoma', 'ileostomy', 'colostomy', 'ostomy', 'Proximal diversion' and 'enterostomy'. The references of eligible studies, previous meta-analyses and reviews were also checked for potential eligible studies in a 'snowball' way. We limited the publication date from 2008/01/01 to 2018/07/29.

Study inclusion

1) Rectal cancer patients; 2) Standard anterior resection (including partial mesorectal excision and total mesorectal excision) with curative intent [9]; 3) Comparative studies among TT, DS and NP. 4) At least one of the following outcomes was provided: anastomotic leakage rate and reoperation rate.

Study exclusion

1) Conlon cancer; 2) Benign tumor; 3) Palliative surgery; 4) Studies focusing on rectal stents; 5) Hartmann surgery and Mile's surgery; 6) Non-English studies; 7) Duplicate studies; 8) Incomplete data; 9) Low quality studies (score ≤ 5 according to Newcastle-Ottawa Scale).

Data extraction

The data extraction was performed by two authors independently, if any disagreements occurred, the third author was consulted. The following information was extracted meticulously from each eligible study: first author, publication year, study design, interventions, sample size, age, male rate, BMI, tumor level, anastomotic leak rate and reoperation rate. If necessary, we tried to contact the corresponding author for missing data. If the data sets were overlapped, only the most recent data was used for our network meta-analysis.

Bias risk assessment

The bias risk of eligible randomized controlled trials (RCT) and cohort studies (CS) were assessed by Cochrane Collaboration's tool for assessing the risk of bias and Newcastle-Ottawa Scale (NOS), respectively. The following terms were used in Cochrane Collaboration's tool for assessing risk of bias: incomplete outcome data, allocation of concealment, selective reporting, random sequence generation, blinding of participants and personnel and blinding of outcome assessment and other sources of bias. The following terms were used in NOS for assessing risk of bias: patient selection, comparability between groups and objectivity of results. If scored

>5 , the cohort study was considered high quality. On the contrary, the cohort study was considered as low quality if it scored ≤ 5 , and was subsequently excluded from our meta-analysis.

Statistical analysis

The effect size of dichotomous variables was expressed by Odds Ratio (OR). The heterogeneity between studies was expressed by I^2 . If $I^2 > 50$, the heterogeneity between studies was assessed as high and the random effects model was used. On the contrary, the heterogeneity between studies was assessed as low and the fixed effects mode was used. The direct meta-analysis was performed by RevMan 5.3 software. The network graph, inconsistency test and comparison-adjusted funnel plot were performed by the Stata 14.0 software. We investigated the consistency within a closed triangular loop by loop-specific approach as previous studies reported [15,16]. We identified consistent loops as those yielding a 95% confidence interval (CI) including 1. The indirect meta-analysis and rank probabilities were performed by the GeMTC R package (version 3.5.1). The Markov chain Monte Carlo Method was used to pool effect sizes [17], and the results were deemed as statistically significant if it did not include value 1. The relative effects of each intervention were converted to the probability that one of specific interventions caused more anastomotic leak and reoperation, and subsequently we ranked the interventions in the order of worst to best, thus performing a league table.

Closed triangular loop

Three treatments connected and formed "Closed triangular loop". It meant that direct and indirect comparisons between 2 treatments existed at the same time. Then it was possible to test the consistency between direct and indirect evidences, which was called consistency test. If there was no line between 2 treatments, it couldn't form a "Closed triangular loop". On this occasion, only indirect evidences existed, and therefore it was impossible to perform Consistency test.

Results

Literature search and characteristics of eligible studies

Our meta-analysis was arranged in line with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Guidelines [18] and its Extension Statement for Network Meta-analyses [19]. After a systematic literature screening of above-mentioned database, a total of 32 studies [6,8,9,12–14,20–45] were included in our network meta-analysis, among which, 6 studies were RCT [6,8,28,29,33,42] and 26 studies were CS [9,12–14,20–27,30–32,34–41,43–45]. The PRISMA flow chart was shown in Fig. 1. The detail characteristics and bias risk assessment of eligible studies were shown in Table 1. A total of 10867 patients were included in our network meta-analysis (1096 patients in the TT group, 4534 patients in the DS group and 5237 patients in the NP group). The RCT proved to be low risk according to Cochrane Collaboration's tool for assessing risk of bias. All eligible CS were found to be high quality according to NOS.

Network graph

Only 1 study made a direct comparison between TT, DS and NP [14]. The geometry of the treatment network was connected forming a triangle. As shown in Fig. 2, the area of the plot represented the patient numbers, while the thickness of the line connecting these plots represented the amount of studies. The network

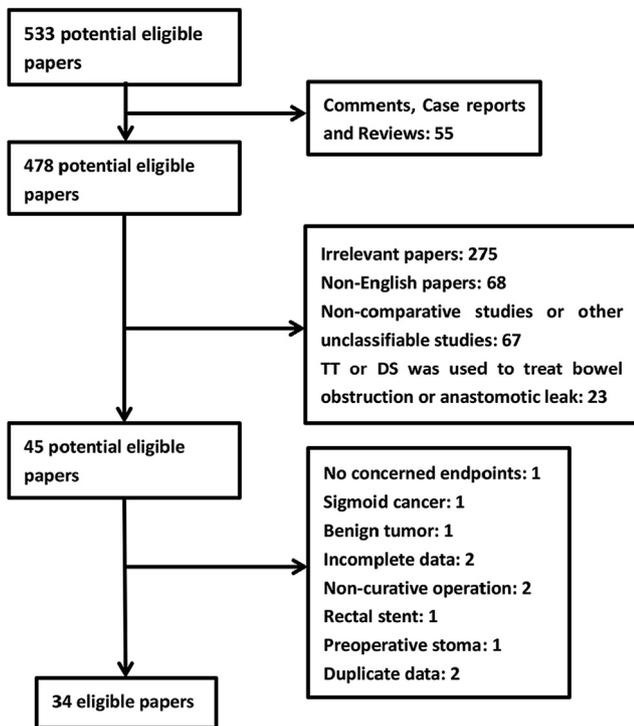


Fig. 1. Flowchart of paper inclusion.

graph regarding anastomotic leakage rate was shown in Fig. 2a, the network graph regarding reoperation rate was shown in Fig. 2b.

Consistency test

There was only one closed triangular loop in our network meta-analysis. The consistency of the closed triangular loop was proven to be satisfactory. The 95% CI of consistency test based on anastomotic leakage rate and reoperation rate were (1, 21.58) and (1, 90.34), respectively.

Direct meta-analysis

10 studies [8,9,14,20–26] made a comparison of anastomotic leakage rate between TT and NP, the forest plot revealed a lower anastomotic leakage rate in the TT group compared with the NP group (Fig. 3). 22 studies [6,12,13,27–45] made a comparison of anastomotic leakage rate between DS and NP: the forest plot revealed a lower anastomotic leakage rate in the DS group compared with the NP group (Fig. 3). 10 studies [8,9,14,20–26] made a comparison of reoperation rate between TT and NP: the forest plot revealed no statistical difference (Fig. 4). 16 studies [12,13,28,30,31,33,35–37,39–43,45] made a comparison of reoperation rate between DS and NP: the forest revealed a lower reoperation rate in DS group (Fig. 4).

Network meta-analysis

The multiple-treatments meta-analyses regarding anastomotic leakage rate and reoperation rate in the order of highest to lowest are summarized in league Table 2. As shown in league Table 2, TT and NP shared equivalent anastomotic leakage rates by showing no statistical difference. Our network meta-analysis also revealed a significantly lower reoperation rate of DS compared with TT.

Rank probabilities

The distribution of rank probabilities of anastomotic leakage rate and reoperation rate are shown in Fig. 5a and Fig. 5b, respectively. As shown in Fig. 5a: the anastomotic leakage rate was the lowest in the TT group, with a probability of 81%; the DS group was associated with a probability of 19%; and the NP group was associated with a probability of 1%. As shown in Fig. 5b: the reoperation rate was the lowest in the DS group, with a probability of 99%; the TT group was associated with a probability of 1%; and the NP group was associated with a probability of 0%.

Publication bias analysis

No obvious publication bias was observed according to the comparison-adjusted funnel plot, based on the anastomotic leakage rate (Fig. 6a). Moreover, according to comparison-adjusted funnel plot based on reoperation rate (Fig. 6b), a clear publication bias was observed.

Discussion

Risk factors for anastomotic leakage

Anastomotic leakage is one of the most feared complications after low anterior resection for rectal cancer. It is hard to predict the anastomotic leakage accurately; however, various factors were reported as risk factors for anastomotic leakage after low anterior resection for rectal cancer, examples included: male sex [46,47], BMI [8], diabetes mellitus [48], ASA score [49], tumor diameter [50], neoadjuvant therapy [2,51], tumor level [2,9,52], long operation time [48], surgical skill [53], absence of DS [54], absence of TT [55] and more. Patients with greater risk factors for anastomotic leakage tended to be selected to receive various procedures preventing anastomotic leakage. In these various procedures, DS was the most popular. However, the routine use of DS was limited due to various drawbacks [6,7]. In recent years, TT placement was introduced to prevent anastomotic leakage after low anterior resection, many studies have proven its favourable outcomes [9–11]. We performed this network meta-analysis with the purpose of making an indirect comparison between TT and DS.

Anastomotic leakage rate

The overall anastomotic leakage rates in our network meta-analysis were 6.5%, 6.2% and 10.7% for the TT group, DS group and NP group, respectively. In the results of our traditional meta-analysis, we proved an obvious lower anastomotic leakage rate in the TT group and DS group compared with the NP group, which was similar to previous meta-analyses [21,56]. The favourable outcomes of TT versus NP were also shown by a number of other comparative studies. Unfortunately, these comparative studies were excluded from our meta-analysis due to inclusion of benign tumors [49] or rectosigmoid tumors [52,57]. In a RCT conducted by Bulow S [58], the rectal stent group shared similar anastomotic leakage rates compared with the NP group, this RCT was also excluded from our meta-analysis because of significant distinctive material of rectal stents compared with TT. One of the most accepted mechanisms of anastomotic leakage after low anterior resection relates to the high intraluminal pressure after anterior resection from the tightly contracted sphincter caused by pain, fear, trauma and inflammation in the early postoperative stage. We speculated that the mechanism for decreasing the risk of anastomotic leakage of TT and DS was the decompression of anastomotic site by bypassing the proximal bowel content. To our best of knowledge, 2 studies compared

Table 1
Patient characteristics and assessment of bias risk.

Author	Year	Study Design	Groups	Sample Size	Age	Male rate	BMI (Kg/m ²)	Tumor Level (cm)	AL	Reoperation	Score
Zanguie M [27]	2018	CS	DS	75	53	61%	NM	NM	1	NM	7
			NP	31	49	58%	NM	NM	6	NM	
Emmanuel A [41]	2018	CS	DS	140	67	66%	26.3	6.8	19	3	7
			NP	63		62%	26.7	7.7	9	9	
Khor BY Ref. [38]	2017	CS	DS	100	NM	69%	26	NM	5	NM	7
			NP	67	NM	49%	27	NM	7	NM	
Flooden H [6]	2017	RCT	DS	116	68	60%	25	10	12	NM	Low risk
			NP	118	67.5	49%	25	10	33	NM	
Mrak K [33]	2016	RCT	DS	94	62.5	63%	26.1	7	6	2	Low risk
			NP	72	63	53%	25.8	9	12	11	
Maroney S [34]	2016	CS	DS	57	62	75%	NM	0–15	3	NM	7
			NP	42	64	76%	NM	0–15	7	NM	
Ihnat P [13]	2016	CS	DS	78	62.8	64%	26.9	9.1	1	0	7
			NP	73	64.1	59%	25.3	9.4	7	5	
Fratric I [12]	2016	CS	DS	47	65	64%	NM	6.6	4	0	7
			NP	102	64	55%	NM	8.9	6	3	
Shiomi A [31]	2015	CS	DS	165	64	65%	22	6	18	1	8
			NP	165	63	70%	22.1	6.5	26	15	
Anderin K [45]	2015	CS	DS	139	62	63%	25	NM	27	3	7
			NP	148	65	57%	25	NM	36	21	
Kim MK [14]	2015	CS	DS	67	32.2	72%	24.3	8.2	5	0	7
			TT	35	62.2	60%	23.7	8.8	1	1	
			NP	35	59.3	66%	22.7	8.9	6	5	
Thoker M [29]	2014	RCT	DS	34	NM	NM	NM	4–12	2	NM	Low risk
			NP	44	NM	NM	NM	4–12	5	NM	
Snijders HS [30]	2014	CS	DS	214	63	41%	NM	10	14	12	7
			NP	72	64	53%	NM	13	7	6	
Bakker IS [44]	2014	CS	DS	1391	66	64%	NM	8	95	NM	7
			NP	657	67	55%	NM	8	66	NM	
Seo SI [32]	2013	CS	DS	246	56	66%	NM	4.6	1	NM	7
			NP	590	58	60%	NM	5.6	26	NM	
Ma CC [35]	2013	CS	DS	30	58	56%	26.2	6.8	2	0	7
			NP	26	58	54%	25.8	7	7	5	
Gong H [40]	2013	CS	DS	26	61.9	38%	NM	4.3	5	2	7
			NP	36	63.3	42%	NM	4.6	0	0	
Beirens K [43]	2012	CS	DS	1183	NM	NM	NM	0–15	51	40	7
			NP	729	NM	NM	NM	0–15	74	69	
Lin JK [36]	2011	CS	DS	145	NM	99%	NM	0–16	8	2	7
			NP	676	NM	62%	NM	0–16	35	35	
Karahasanglu T [39]	2011	CS	DS	23	59	65%	28.4	NM	0	0	7
			NP	54	61	46%	24.7	NM	3	3	
Ulrich AB [28]	2009	RCT	DS	18	62	61%	26.6	8	1	0	Low risk
			NP	16	60	63%	25.4	7	6	6	
Lefebure B [37]	2008	CS	DS	42	69	50%	30	0–8	3	0	7
			NP	90	68.4	61%	26	0–8	10	5	
Chude GG [42]	2008	RCT	DS	136	55.5	56%	NM	0–5	3	0	Low risk
			NP	120	55.5	55%	NM	0–5	12	2	
Kawada K [23]	2018	CS	TT	178	NM	NM	NM	NM	19	10	7
			NP	23	NM	NM	NM	NM	6	3	
Goto S [25]	2017	CS	TT	205	67	70%	22	8	17	7	7
			NP	123	70	63%	22.7	10	19	8	
Yang CS [21]	2016	CS	TT	102	64.2	64%	23.9	7.9	10	4	8
			NP	102	63.5	65%	23.5	7.8	12	12	
Hidaka E [24]	2015	CS	TT	96	63.4	67%	21.2	4.5	4	0	7
			NP	109	64.6	60%	21.8	6	15	10	
Lee SY [22]	2015	CS	TT	154	63.6	67%	24.1	NM	9	8	7
			NP	382	68.2	66%	23.8	NM	41	30	
Nishigori H [9]	2014	CS	TT	36	61	64%	22	7	1	1	7
			NP	140	63	63%	22.4	8	22	11	
Adamova Z [26]	2014	CS	TT	9	65	33%	NM	NM	0	0	7
			NP	57	64	49%	NM	NM	5	5	
Zhao WT [20]	2013	CS	TT	81	NM	58%	NM	NM	2	2	7
			NP	77	NM	56%	NM	NM	7	7	
Xiao L [8]	2011	RCT	TT	200	59	58%	24.2	7	8	2	Low risk
			NP	198	58	61%	23.7	8	19	16	

CS = cohort study; RCT = randomized control trial; DS = defunctioning stoma; NP = non-protection; TT = transanal tube; NM = not mentioned; BMI = Body Mass Index; AL = anastomotic leakage.

intraluminal pressure by anal manometry, and both studies showed an obvious lower intraluminal pressure in the TT group compared with the NP group [8,59]. In our results of network meta-analysis, no statistical difference was found regarding anastomotic leakage

rate between the TT and DS, which indicated that TT may be an alternative procedure of DS. Even though DS was the most popular procedure decreasing the risk of anastomotic leakage after anterior resection, various drawbacks cannot be ignored, such as: stoma-

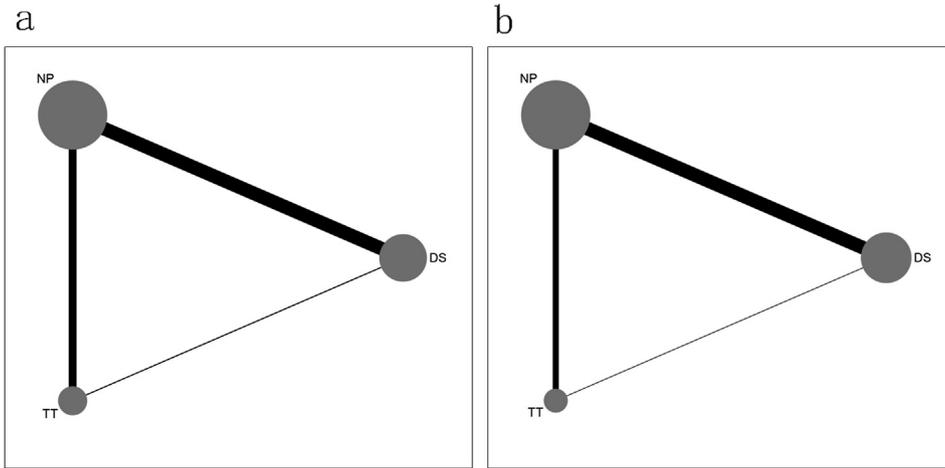


Fig. 2. a) Network graph of included studies regarding anastomotic leakage; b) Network graph of included studies regarding reoperation rate. The area of the plot represented the patient numbers, while the thickness of the line connecting these plots represented the amount of studies.

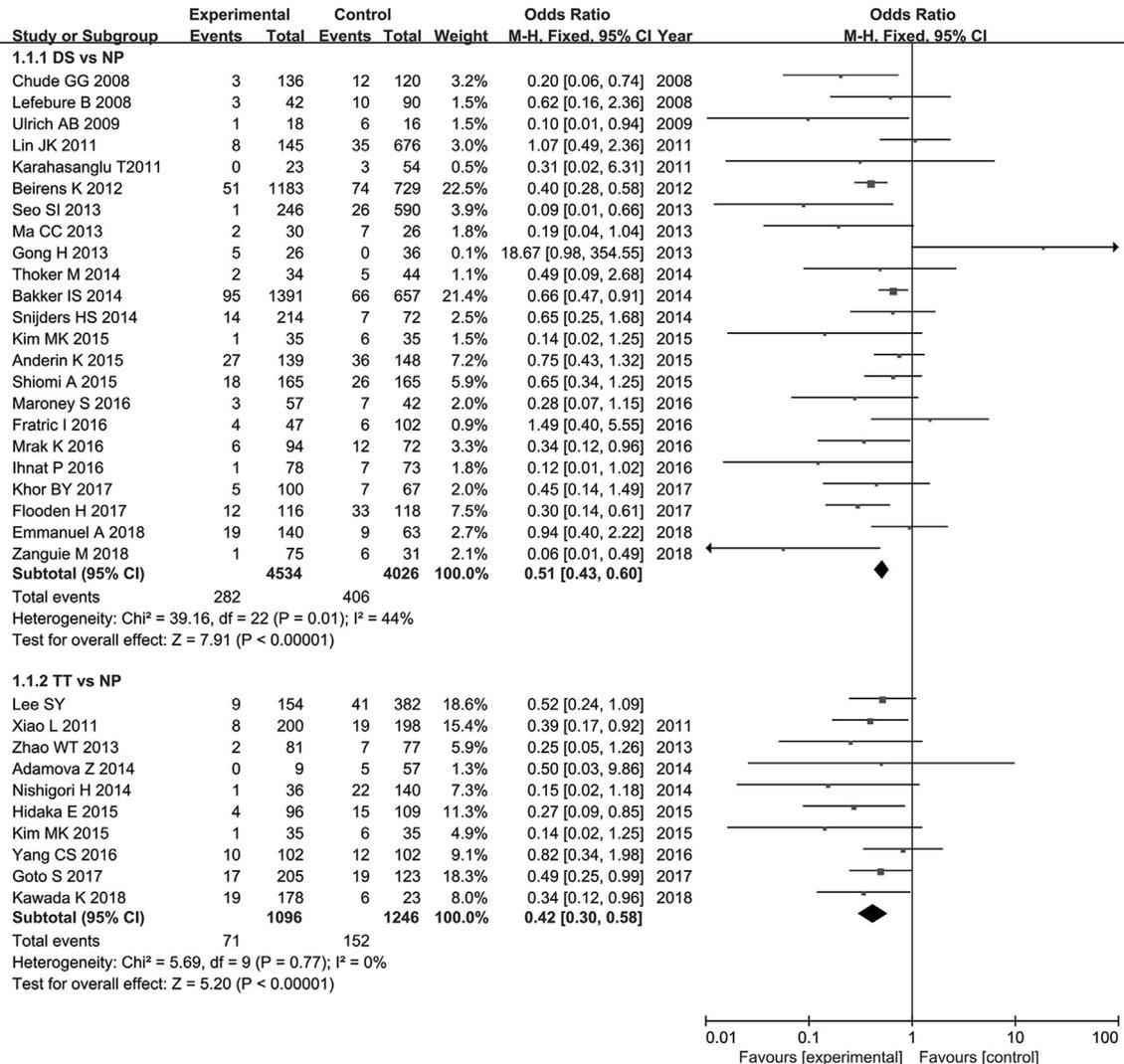


Fig. 3. Direct meta-analysis regarding anastomotic leakage rate.

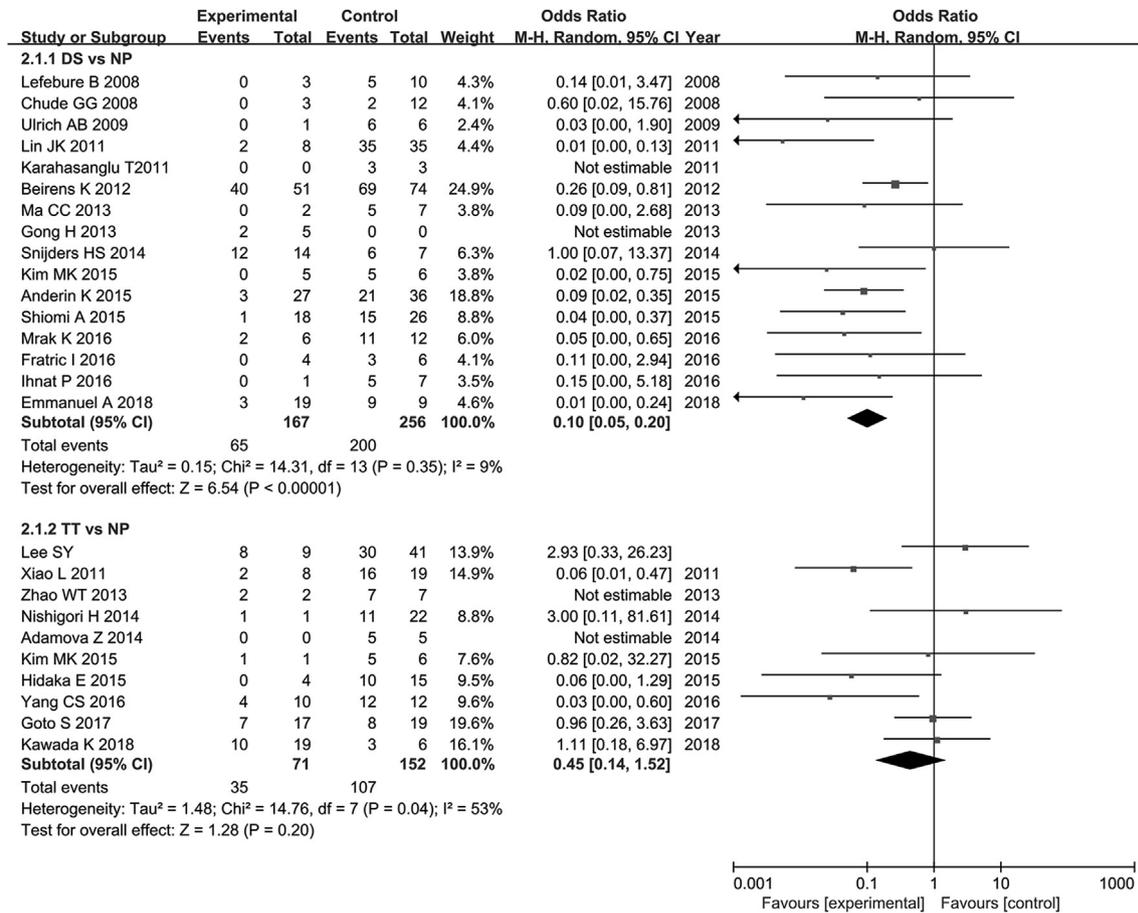


Fig. 4. Direct meta-analysis regarding reoperation rate.

Table 2
League table regarding anastomotic leakage rate and reoperation rate.

Anastomotic leakage		
NP		2.10 (1.60, 2.89)
0.48 (0.35, 0.63)	DS	0.38 (0.23, 0.58)
2.62 (1.71, 4.33)	TT	0.80 (0.47, 1.33)
		1.25 (0.75, 2.15)
Reoperation		
NP		0.38 (0.03, 5.55)
2.65 (0.18, 39.42)	TT	145.95 (18.19, 3614.00)
0.01 (0.00, 0.05)	DS	53.44 (2.64, 4603.69)
		0.02 (0.00, 0.38)

We ranked the treatments in the order of highest to lowest regarding anastomotic leakage rate and reoperation rate. The results were deemed as statistical significant if it did not include value 1. NP = non-protection; DS = defunctioning stoma; TT = transanal tube.

related morbidity and mortality, requirement for reoperation, longer hospital stay, greater hospitalization costs as well as inconvenience [6]. More importantly, previous studies have reported a 15% incidence of failing to achieve stoma reversal because of anastomotic stenosis [7]. As an instrument of bypassing proximal bowel content and decompression of intraluminal pressure, TT was also suggested to treat abdominal distension after colonoscopy [60]. Some authors even used TT to treat anastomotic leakage [61], which further reinforced our results. Compared with DS, TT is cheaper and technically simpler. For this reason we suggest the routing use of TT for decreasing the risk of anastomotic leakage after anterior resection.

Reoperation rate

The overall anastomotic leakage-related reoperation rates in our

network meta-analysis were 49.3%, 39% and 75.2% for the TT group, DS group and NP group, respectively. In the results of our traditional meta-analysis, we proved a clear lower reoperation rate in the DS group compared with the NP group, which was consistent with previous meta-analyses [56,62]. Our results also showed the lower reoperation rate in the TT group than the NP group, even though no statistical difference was found, which was inconsistent with previous meta-analyses [11,63]. When pooling the reoperation rate, “patients with anastomotic leakage” was used as “total” in our study, while “whole patients” was used as “total” in previous meta-analyses, which may explain the different result between our study and previous meta-analyses [11,63]. Reoperation rate was an indicator reflecting the severity of anastomotic leakage. In view of this point, our results may be more reliable. In our results of network meta-analysis, the reoperation rate was significantly lower in DS compared with TT, which indicated the reduced severity of

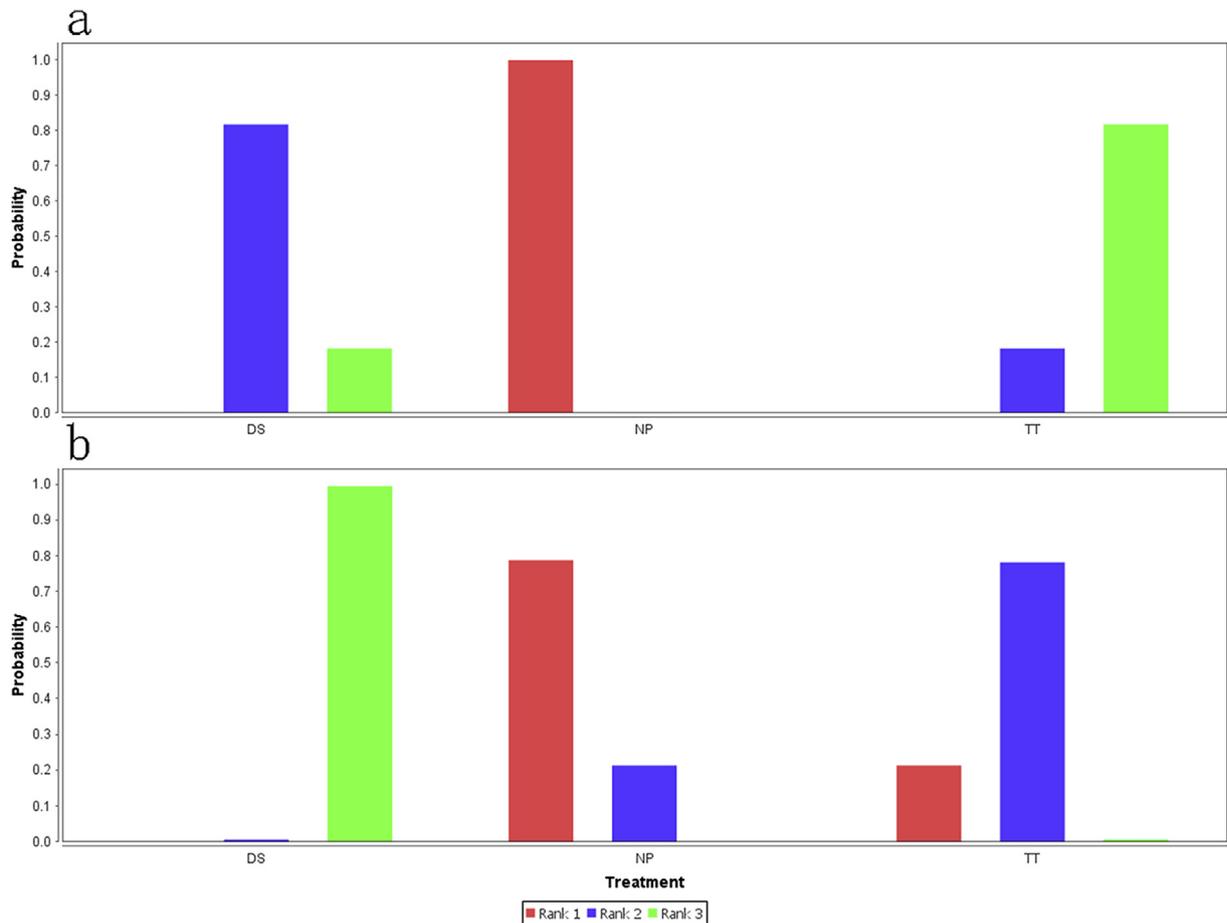


Fig. 5. a) Distribution of probabilities of anastomotic leakage rate being ranked at each of the possible positions. b) Distribution of probabilities of reoperation rate being ranked at each of the possible positions.

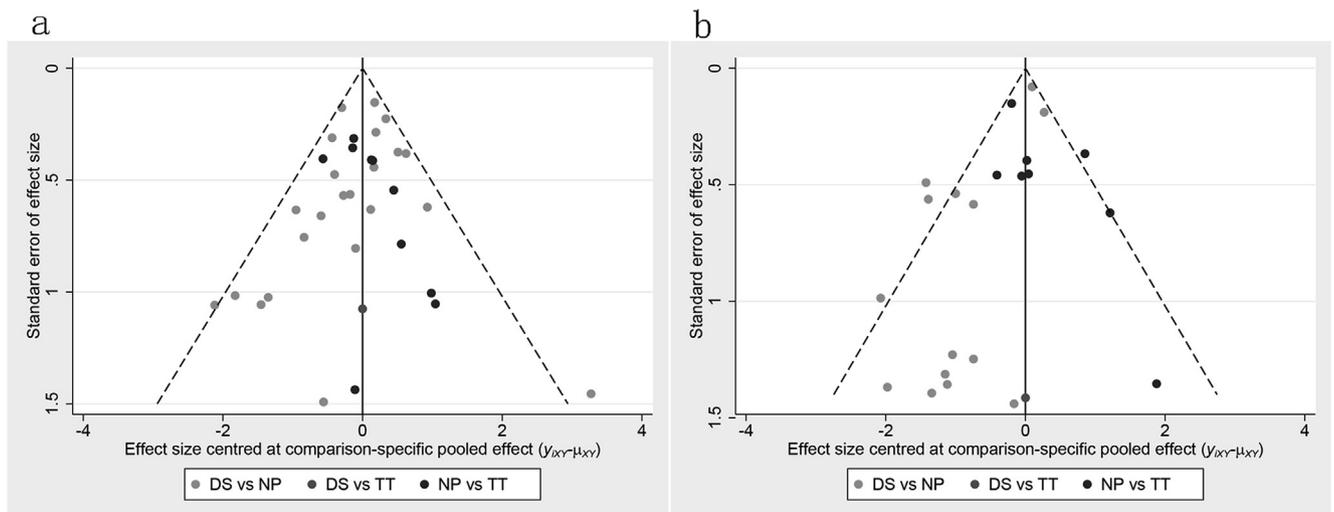


Fig. 6. a) Comparison-adjusted funnel plot regarding anastomotic leakage rate. b) Comparison-adjusted funnel plot regarding reoperation rate.

anastomotic leakage in DS compared with TT. In case of anastomotic leakage, TT and DS could drain or bypass the bowel content effectively. Hence only little bowel content was extracted out of the defect site of anastomosis, which may be cured conservatively. However, the effectiveness of TT on draining bowel content was restricted by its relatively narrower internal diameter than that of

DS. Additionally, TT may be clogged by the solid feces in some cases. Based on these points, the lower reoperation rate in the DS group compared with the TT group could be explained reasonably. It could be observed from Table 1 that even though DS existed, some patients with anastomotic leakage still required reoperation, which indicated that DS was just a procedure decreasing the risk of

anastomotic leakage-related reoperation instead of a procedure avoiding anastomotic leakage-related reoperation completely.

Some technical aspects

TT was reported to measure the fecal volume, which could be used to predict anastomotic leakage after anterior resection [23]. The authors proved significantly higher anastomotic leakage rates after anterior resection in patients whose daily fecal volume exceeded 100 ml/day in two or more days than that of those in 0 or 1 day (26.9 vs. 7.9%) [23]. TT was also reported to treat anastomotic leakage [61], bowel obstruction [64] and abdominal distension after colonoscopy [60]. There were also several limitations of TT, which must be considered. TT placement can cause discomfort and skin problems in the anal region. Additionally, TT placement makes postoperative ambulation more challenging, which may increase the complications of pneumonia and thrombosis [25].

Limitations

Our meta-analysis was still subject to several limitations. Firstly, most of our eligible studies were non-RCTs with inherent selection bias. Patients with a greater number of risk factors for anastomotic leakage tended to be treated with DS, which may have influenced the reliability of our results. Secondly, the 2 most popular procedures of DS were ileostomy and colostomy. However, we did not distinguish them in our meta-analysis because few eligible studies made a distinction between ileostomy and colostomy. Thirdly, the funnel plot regarding reoperation rate was asymmetric, which may be explained by the various indications of reoperation when anastomotic leakage occurred in different hospitals.

Conclusion

Both TT and DS were protective factors of anastomotic leakage after anterior resection for rectal cancer. DS reduced severity of anastomotic leakage in a more effective way than TT. However, we still suggested the routing use of TT for decreasing the risk of anastomotic leakage in anterior resection because it was cheaper and technically simpler.

Ethics statements

Our study was approved by the Ethics Committee of Hospital.

Conflict of interest

None.

Declarations of interest

All authors report no conflict of interests.

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none.

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