



The influence of intraoperative rectal washout on local recurrence of colorectal cancer following curative resection: a systematic review and meta-analysis

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Abstract

Purpose To determine the effectiveness of rectal washout in preventing local recurrence of distal colorectal cancer following curative resection.

Methods A systematic review and meta-analysis was performed after a literature search was conducted on MEDLINE, EMBASE, the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP), ClinicalTrials.gov, and the ISRCTN registry. The study was reported using PRISMA guidelines. The primary endpoint was incidence of local recurrence of cancer after distal colonic and rectal cancer surgery.

Results After screening, 8 studies with a total sample size of 6739 patients were identified. At 5-year follow-up, local recurrence in the washout group (WO) was 6.08% compared to 9.48% in the no-washout group (NWO) group (OR 0.63, 95% CI=0.51–0.78, $\text{Chi}^2=6.76$, $df=7$, $p=0.45$). The relative risk reduction was 36.9%. To exclude a 36.9% relative risk reduction from 9.48 to 6.08% with a 5% significance level and 80% power a randomized control trial would require a total sample size of 1946 participants distributed equally between the two treatment arms.

Conclusion It is safe to recommend the use of rectal washout for left sided and rectal tumour resections. It is a simple and safe step during colorectal surgery that appears to improve long-term oncological outcomes and was not reported to be associated with any complications.

Keywords Rectal washout · Local recurrence · Colorectal cancer · Rectal tumour · Washout · Lavage

Introduction

Colorectal cancer is the 4th most prevalent cancer in the UK with 43,729 new cases diagnosed in 2017 and a mean 5-year survival rate of 58.4% [1]. Local recurrence following surgical resection has been reported to occur in 5 to 19% of patients [2–4].

Local recurrence is defined as the presence of recurrent tumour at the anastomotic site, peri-rectally, at the stoma site or in the lesser pelvis, which includes invasion of the bladder, vagina and pelvic lymph nodes.

Implantation of exfoliated tumour cells into local tissue is thought to contribute to local recurrence [5, 6]. This

occurs as a result of trauma to the bowel and surrounding tissues during surgery and during formation of the anastomosis [7–11]. Historical data suggests that stapling devices introduced trans-anally increase the risk of local recurrence compared with hand sown techniques [11, 12]. This is especially pertinent in contemporary laparoscopic and open rectal cancer surgery where the use of staplers is commonplace.

Rectal washout involves cross-clamping the rectum distal to the identified tumour. An irrigation system or 50-mL syringe is used to irrigate the rectum distal to the cross-clamp, flushing intraluminal content. The rectum is then transected distal to the already placed cross-clamp.

In 2005, the American Society of Colorectal Surgeons (ASCS) published practice guidelines, which suggested that there is insufficient evidence to recommend rectal washout. In 2008 a meta-analysis was unable to reach a definitive conclusion due to a scarcity of available data. The association of coloproctology of Great Britain & Ireland (ACPGBI) [13] published guidelines in 2017 on the management of cancers

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of the colon and rectum and reported “Cytocidal washout of the rectal stump should be used prior to anastomosis.— Recommendation grade B”. Since then, several papers have been published on this topic. Accordingly, we performed a systematic review and meta-analysis of the influence of rectal washout on local recurrence after curative distal colonic and rectal resection for cancer.

Methods

PICO statement: In patients who have undergone curative surgical resection of distal colorectal cancer, does intra-operative rectal washout versus no rectal washout, reduce the rate of local recurrence of cancer?

A literature search was conducted using MEDLINE (1946–2020), EMBASE (1980–2020). To identify ongoing trials, a further search was conducted using the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP), ClinicalTrials.gov and the ISRCTN registry. The search yielded a total of 323 abstracts. References of relevant systematic reviews were screened for other potential studies yielding 5 further abstracts.

Two authors (JS and TM) independently reviewed the titles and abstracts of articles identified in the search and independently extracted data using a piloted data extraction form. In cases where the two primary authors are unable to reach a unanimous decision regarding inclusion of a study the final decision is made by a third reviewer (JW).

Search terms included “left sided tumours”, “rectal cancer”, “rectal neoplasm”, “rectal malignancy”, “rectal tumour”, “washout”, “lavage”, “toilet”, “irrigation”, “seeding”, “local recurrence”, “anastomotic recurrence” and “cancer recurrence” were used. Both free text and MeSH terms were used in the formal literature search.

All randomised control trials, prospective and retrospective cohort studies were considered for inclusion. All studies looked at elective resection of recto-sigmoid tumours by an anterior resection or Hartmann’s procedure, laparoscopic or open. Participants had to be adults over the age of 18.

Exclusion criteria included abdomino-perineal resections, operations with palliative intent and operations performed as an emergency. Only papers with original text written in English were considered eligible for inclusion.

Quantitative data were analysed using RevMan (version 5.3). The Cochrane Collaboration. Two review authors (JS and TM) achieved consensus on which data to extract and include for quantitative analysis. For each comparison, summary estimates of treatment effect together with 95% confidence intervals (CIs) were calculated for individual outcomes. Dichotomous outcomes were reported as odds ratios (OR). The Mantel–Haenszel method was used to combine

the odds ratio for the outcomes of interest using a “random effects” meta-analytical technique.

Where two or more studies were deemed to be clinically homogenous, the pooled data were assessed for statistical heterogeneity using RevMan. Heterogeneity was assessed by visual inspection of the forest plot along with the test for heterogeneity and the *I*² statistic [14]. Power calculation for the primary outcome used an alpha = 0.05 and power (1-beta) of 0.8. All included studies were assessed for risk of confounding and selection bias.

Review methods followed the AMSTAR2 protocol and were established prior to the conduct of the review and submitted for clinical trial registration. There were no significant deviations from the specified protocol.

Results

Three hundred and twenty-three articles were identified during the database search. Nineteen studies compared WO versus NWO on the rate of local recurrence. Seven of these were meta-analyses and were excluded; one was a non-comparative study and three studies were not available as full text in English (Table 1). Eight studies were included in the quantitative synthesis (Fig. 1). There were no available randomised control trials. All included studies were prospective or retrospective non-randomised cohort studies or case control studies. Included studies were assessed for risk of bias using the ROBIN-I tool (Fig. 2).

A total of 6739 patients were included with 4963 in the WO group and 1776 in the NWO group (Table 2). The average follow-up period was 58.2 months (range 48–60). The mean age of participants was 65.9. All studies matched groups for age and gender, with 5 out of 8 studies matched for Dukes’ stage. However, 2 of the remaining 3 studies matched TNM stage in place of Dukes’.

Table 1 Excluded studies

Study ID	Reason for exclusion
Constantinides et al. [3]	Meta-analysis
Jenner et al. [25]	Non comparative study
Kawahara et al. [26]	Non-English paper
Matsuda et al. [27]	Meta-analysis
Nakano et al. [28]	Non-English paper
Pattana-arun and Wolff [29]	Meta-analysis
Rondelli et al. [30]	Meta-analysis
Sidiqqi et al. [31]	Meta-analysis
Shinto et al. [32]	Non-English paper
Zhou et al. [33]	Meta-analysis
Zhou et al. [33]	Meta-analysis

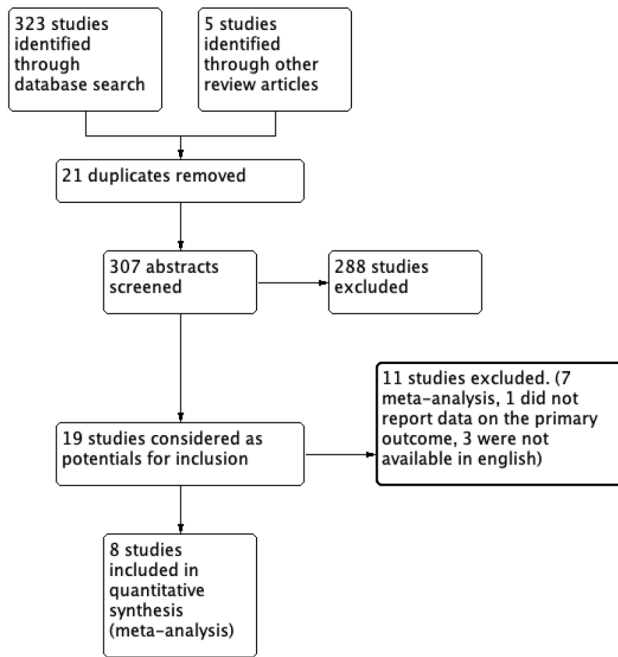


Fig. 1 PRISMA flow diagram for search results

At 5-year follow-up, local recurrence in the WO group was 6.08% compared to 9.48% in the NWO group OR 0.63, 95% CI = 0.51–0.78, $\chi^2 = 6.76$, $df = 7$, $p = 0.45$ (Fig. 3).

	Bias due to confounding	Bias of selection of participants into study	Bias of classification of interventions	Bias due to deviations from intended interventions	Bias in measurement of outcomes	Bias in selection of the reported result
Agaba 2004	?	?	+	+	+	+
Fukuda 1991	?	?	+	+	+	+
Jorgen 2016	+	?	+	+	+	+
Kodeda 2010	+	+	+	+	+	+
Long 1989	?	?	+	+	+	+
Moosvi 2018	+	?	+	+	+	+
Terzi 2006	-	?	+	+	+	?
Xingmao 2013	-	-	+	+	+	+

Fig. 2 Risk of bias assessment (ROBIN-I Tool 2016)

On the basis of this study, we found that the number needed to treat would be 29 (95%CI 20.9–56.6) in order to prevent 1 local recurrence at 5 years.

The relative risk reduction was 36.9%. To exclude a 36.9% relative risk reduction with a 5% significance level and 80% power, a randomized control trial would require a total sample size of 1946 participants distributed equally between the two treatment arms.

A sensitivity analysis of the included studies was carried out. Studies at high risk of bias (Terzi [31] and Xingmao and Jianjun [32]) were excluded from meta-analysis to see whether this had an influence on the overall result. OR 0.62 95% CI (0.50–0.77). There was little significant difference in the overall results.

Discussion

The principal finding of this study was that rectal washout was associated with favourable outcomes for patients undergoing distal colonic or rectal cancer surgery. Indeed 6 out of the 8 included studies reported favourable outcomes when rectal washout was used, the other two studies found there was no significant difference.

The overall rate of recurrence in this study is 7.0%; in line with that reported previously (5–19%) [2–4]. The majority of study participants in this meta-analysis were recruited from two large non-randomised retrospective cohort studies; Jorgen et al. [15] containing 1180 participants [14] and Kodeda et al. with 4600 [16]. The percentage of participants within these two Swedish studies who received rectal washout was 72% emphasising the widespread application of rectal washout within Sweden. These two large studies presented conflicting results. Jorgen et al. reported that washout did not significantly improve local recurrence, distant metastases, or 5-year overall survival. However, Kodeda et al. reported lower rates of local recurrence in patients that had rectal washout. In Kodeda et al., the no washout group (NWO) showed significantly lower rates of preoperative radiotherapy (41% vs 50%) which may have contributed as a confounding variable in the results.

Local recurrence can theoretically occur in two ways; incomplete resection or spillage of viable cancer cells into the surgical field, which implant into surrounding tissue [5, 6, 17, 18]. In principle, rectal washout reduces the number of viable cancer cells within the bowel lumen through irrigation and cytocidal effect and minimizes the risk of implantation. A trial in 2013 [19] found that washout retrieved viable malignant cells from intraluminal effluent on microscopy in 90% of patients ($p = 0.026$). This adds weight to the theory that rectal washout can reduce the number of malignant cells near the surgical field at the time of surgery.

Table 2 Included study characteristics and demographics

Study ID	Study type	Washout solution	Number of patients		Local recurrence rate (LRR%)		Mean age (WO/NWO, years)	Duration of follow-up years	Study characteristics	
			Total	Washout (WO)	No washout (NWO)	LRR WO %				LRR NWO
Agaba [34]	RNR	Cetrimide 1%	141	90	51	4.4	5.9	63.0/61.0	60	1,2,5–11
Fukuda et al. [35]	PNR	NaCl 0.9%	135	26	109	0.0	11.0	NR	48	1,2,5,6,8
Jorgen et al. [36]	RNR	NR	1188	686	502	7.1	9.8	77.0/78.0	60	1,2,6,11
Kodeda et al. [37]	RNR	NR	4600	3749	851	6.0	9.9	69.0/70.0	60	1,2,5–7,11
Long and Edwards [38]	PNR	Formalin 1%	40	12	28	8.3	28.5	NR	60	1,2,4
Moosvi et al. [39]	PNR	Cetrimide, chlorhexidine	395	297	98	5.7	4.0	69.4/68.2	60	1,2,5,8,10,11
Terzi et al. [40]	PNR	Povidone-iodine 5%	96	38	58	7.8	3.4	59.6/61.8	36	1,2,5–10
Xingmao and Jiangjun [41]	PNR	NaCl 0.9%	144	65	79	4.3	6.6	56.3/59.0	60	1,2,6–8,11
Total			6739	4963	1776			65.7 avg/66.3 avg	55.5 (36–60)	

Matching criteria: 1 age, 2 gender, 3 body mass index (BMI), 4 America Society of Anaesthesiologists (ASA) grade, 5 Duke's stage, 6 TNM stage, 7 tumour grade, 8 distance from anal verge, 9 radial resection margin, 10 residual tumour status, 11 neoadjuvant/adjuvant therapy

RNR retrospective non-randomised, PNR prospective non-randomised, NR not recorded, WO washout, NWO no washout

Study or Subgroup	Weight	Odds Ratio	
		M-H, Random, 95% CI	
Agaba 2004	1.8%	0.74	[0.16, 3.46]
Fukuda 1991	0.5%	0.15	[0.01, 2.57]
Jorgen 2016	25.3%	0.71	[0.47, 1.08]
Kodeda 2010	64.6%	0.58	[0.44, 0.75]
Long 1989	0.9%	0.23	[0.03, 2.06]
Moosvi 2018	3.5%	1.43	[0.47, 4.35]
Terzi 2006	1.3%	2.40	[0.38, 15.09]
Xingmao 2013	2.0%	0.64	[0.15, 2.77]
Total (95% CI)	100.0%	0.63	[0.51, 0.78]
Total events			
Heterogeneity: Tau ² = 0.00; Chi ² = 6.76, df = 7 (P = 0.45); I ² = 0%			
Test for overall effect: Z = 4.31 (P < 0.0001)			

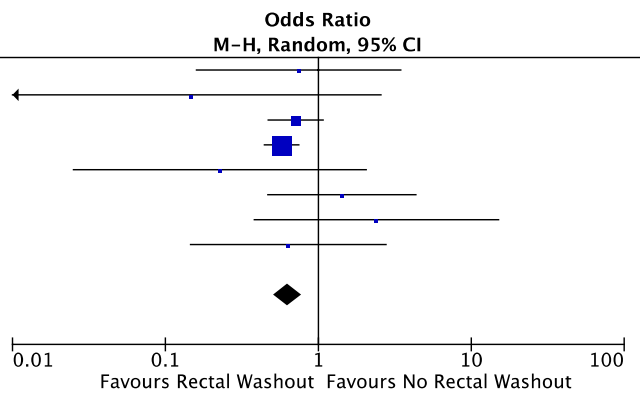


Fig. 3 Meta-analysis: effect of rectal washout on local recurrence

Advances in surgical practice including total mesorectal excision (TME) have significantly improved outcomes for patients by reducing local recurrence [20]. It is important to note that rectal washout was an essential step in the TME technique described by Heald [21].

One systematic review published in 2013 [21] conducted sub-group analysis on rectal washout and TME; it found that rectal washout significantly reduced the risk of local recurrence irrespective of whether the patient had TME excision or not. Indeed, rectal washout was found to have comparable effect to neoadjuvant radiotherapy in reducing local recurrence. Kodeda et al. conducted further subgroup analysis on patients who received neo-adjuvant radiotherapy and found that rectal washout was still beneficial in reducing local recurrence in this cohort of patients (4.5% vs 7.1% $p=0.04$) [18].

Literature proves that advances in oncological surgical practice, increasing usage of TME, neo-adjuvant therapies and adjuvant therapies, have greatly improved outcomes for patients. However, local recurrence continues to blight colorectal oncological surgery. Our review concludes that rectal washout improves outcomes when TME and neoadjuvant radiotherapy are excluded as confounding variables.

All included studies were non-randomised and were therefore at particular risk of confounding and selection bias. Some papers mitigated this risk by the inclusion of strict matching criteria and regression analyses—the matching criteria of each study can be found Table 2. Terzi and Xingmao were judged to be of particular high risk of confounding due to incomplete matching criteria including failure to report use of adjuvant therapies or resection margin status. Seven of 8 included studies were at risk of selection bias due to failure to report how a participant was allocated to a treatment arm. Risk of reporting bias and measurement of outcomes were very low overall. Risk of publication bias was explored by constructing a funnel plot (Fig. 4). A comprehensive search of unpublished data and grey literature was also performed. Studies that were not available in English

language could not reliably be assessed for methodological quality or biases and were therefore excluded from this systematic review. There were 3 such studies found through search with a combined sample size of 363 participants. It is unclear if the exclusion of this data would have impacted the overall findings of this review.

This study is limited by the lack of randomised control trials addressing rectal washout, with unavoidable risks of selection bias and confounding. There was significant heterogeneity of included studies, with a variety of irrigation solutions and volumes used (Table 2). It remains unclear whether the solution type or volume impacts efficacy. Similarly, there was no consistency of surgical technique, which was largely dependent on the experience of the operating surgeon. The use of neo-adjuvant radiotherapy and adjuvant chemotherapy was determined on a case-by-case basis at multi-disciplinary team (MDT).

There were no reported adverse events associated with the use of rectal washout [3, 23]. The number needed to treat (NNTT 29.3) is therefore acceptable when taking into consideration the relative ease of the procedure, safety and overall cost and time added to the operation.

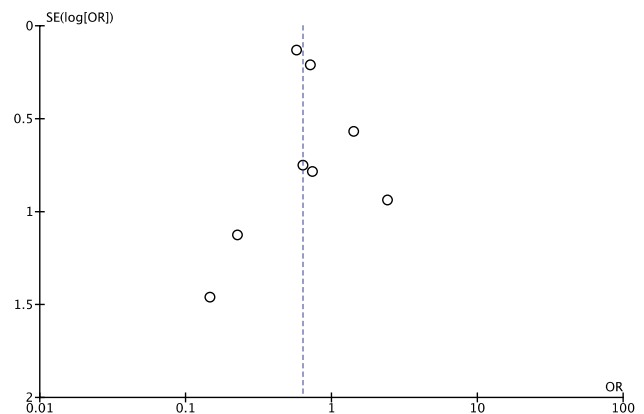


Fig. 4 Funnel plot of local recurrence

The authors conclude that it is safe to recommend the use of rectal washout for left-sided and rectal tumour resections until such time that data from a randomised control trial is available. An assessment of the certainty of evidence was conducted according to GRADE decision framework [22]. A Grade B recommendation was made. There are recognised technical limitations in implementing rectal washout in laparoscopic and robotic surgery. New innovations like an integrated irrigation system described by Rondelli et al. [24] may be useful in the future to help overcome this barrier.

A randomised control trial with a comparison of several irrigation solutions looking specifically at TME procedures with elective, curative resections with clear resection margins (R0) would be invaluable in determining the true effect of local washout. Power calculations dictate this would require 1946 participants and a 5-year follow-up period. Furthermore, many surgeons hold anecdotal views on the importance of rectal washout presenting an ethical challenge to its omission. A survey conducted through Association of Coloproctology of Great Britain and Ireland (ACPGBI) would illustrate common clinical practice in the UK and help to establish equipoise.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s00384-021-04071-w>.

Data availability On written request.

Declarations

Ethical approval Not applicable.

Patient consent Not applicable.

Permission to reproduce material from other sources Not applicable.

Consent to participate Not applicable.

Consent for publication Not applicable.

Conflict of interest The authors declare no competing interests.

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Included studies

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