

# Water exchange versus air insufflation for colonoscopy: A meta-analysis

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## Abstract

**Background/Aims:** To compare water exchange (WE) method with conventional air insufflation (AI) method for colonoscopy, evaluating the technical quality, screening efficacy, and patients' acceptance.

**Materials and Methods:** Electronic databases were systematically searched for randomized controlled trials comparing WE colonoscopy with AI colonoscopy. The pooled data of procedure-associated and patient-related outcomes were assessed, using the weighted mean difference (WMD) with 95% confidence interval (CI) for continuous variables and relative risk (RR) with 95% CI for dichotomous variables, respectively.

**Results:** A total of 13 studies involving 7056 patients were included. The cecum intubation rate was similar between WE and AI methods (RR = 1.01, 95% CI = 0.99–1.02,  $P = 0.37$ ); however, a significantly longer cecum intubation time was shown in WE group (WMD = 1.56, 95% CI = 0.75–2.37,  $P = 0.002$ ). Compared with AI, WE was associated with a higher risk of adenoma detection rate (ADR) (RR = 1.28, 95% CI = 1.18–1.38,  $P < 0.00001$ ) and polyp detection rate (PDR) (RR = 1.30, 95% CI = 1.21–1.39,  $P < 0.00001$ ). Patients in WE group experienced significantly less maximum pain score (WMD = -1.99, 95% CI = -2.68 to -1.30,  $P < 0.00001$ ) and less requested on-demand sedation (RR = 0.58, 95% CI = 0.44–0.77,  $P = 0.0002$ ). Likewise, they also experienced less abdominal compression (RR = 0.62, 95% CI = 0.51–0.74,  $P < 0.00001$ ) and reposition (RR = 0.74, 95% CI = 0.63–0.86,  $P = 0.0001$ ). Moreover, patients' willingness to repeat colonoscopy was significantly greater for WE (RR = 1.14, 95% CI = 1.07–1.21,  $P < 0.0001$ ).

**Conclusion:** This meta-analysis confirmed that WE method could significantly increase ADR/PDR and improve patients' acceptance of colonoscopy, while reducing the degree of pain and minimize the need for on-demand sedation and adjunct maneuvers, despite requiring more cecal intubation time.

**Keywords:** Air insufflation, colonoscopy, meta-analysis, water exchange

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## INTRODUCTION

Colonoscopy remains the cornerstone examination for the diagnosis, surveillance, and treatment of colorectal diseases.<sup>[1]</sup> It is usually performed with standard air insufflation (AI) which distends the colonic lumen to permit visualization

and passage of the instrument. Usually, AI colonoscopy is considered to be painful and poorly tolerated procedure for most patients without sedation. The undesirable outcomes are partly due to colon distension, angulations' exaggeration at flexures, and looping of the instrument. All these expose patients to potential risks (e.g., perforation, bleeding).<sup>[2]</sup>

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Due to the relatively low cecal intubation rate and intolerable pain, sedation has generally been recommended for AI colonoscopy. However, sedated colonoscopy is associated with additional risk of sedatives, higher medical costs, and a longer recovery time compared with unsedated colonoscopy.<sup>[3]</sup> Therefore, any endoscopic technique that minimizes the sedation needs has the potential to improve the quality of the procedure.

Water infusion method is gaining increasing interest in recent years. Compared with AI method, the water infused opens colonic lumen and weighs down the left colon to straighten the sigmoid segment, thus facilitating the advancement of colonoscope and reducing insertion pain and discomfort.<sup>[4]</sup> Water infusion methods are mainly classified as water immersion (WI) and water exchange (WE). They are distinguished by removal of the infused water during withdrawal (WI) or insertion (WE).<sup>[5]</sup> When performed with WE, removal of the infused water in addition to suction residual feces and retained air may maximize the cleanliness of the colonic lumen, which is supposed to have a superior impact on colonoscopy than WI.<sup>[6]</sup>

Recently, considerable new data related to WE method instead of AI have been generated by investigators worldwide. These clinical studies have shown that WE is an attractive strategy used in colonoscopy as it can minimize sedation requirement, increase disease detection rate, and improve patients' acceptance of the procedure without compromising the success rate of cecal intubation.<sup>[7-10]</sup> Despite evidence in support of WE for improving the quality of colonoscopy, there are still some reservations among endoscopists regarding its true benefits.<sup>[11]</sup>

The aim of this meta-analysis was to investigate the effects of WE method compared with conventional AI method used in colonoscopy, in terms of procedure-associated and patient-related outcomes.

## SUBJECTS AND METHODS

### Study identification

This study was performed according to the standard guidelines for meta-analyses and systematic reviews of randomized controlled trials (RCTs). Medline, Embase, Cochrane Library, and ISI Web of Knowledge were searched systematically for RCTs published up to December 2017 concerning the water method in colonoscopy, using the terms "water" and "colonoscopy." The reference lists were also inspected for relevant studies.

### Study selection and quality assessment

Eligible studies were included in the meta-analysis if they met the following criteria: (1) full-text RCTs published in English; (2) patients undergoing colonoscopy; (3) using WE or AI method; (4) outcome measures including procedure-associated or patient-related data; and (5) allowing no AI any time during insertion in the water group.

Exclusion criteria were as follows: (1) any comment, review, or guidelines were excluded; (2) colonoscopy procedures conducted by trainees; (3) using carbon dioxide or other gas insufflations; (4) using WI technique; and (5) using water infusion technique combined with AIs.

Study quality was assessed using Cochrane Risk of Bias Tool (based on a description of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective report and other bias).

### Data extraction and synthesis

Two of the authors (Y.L. and Q.-K.H.) performed study selections independently and reached consensus on all items. Data were extracted as follows: first author, publication year, country, number of patients, water temperature, water volume, cecal intubation time, cecal intubation rate, ADR/PDR, maximum pain score during the procedure, on-demand sedation rate, need for abdominal compression or position change, and willingness to undergo a repeat colonoscopy. For summary statistics in meta-analyses, we calculated the pooled relative risk (RR) for dichotomous data using intention-to-treat analysis and weighted mean difference (WMD) for continuous data using per-protocol analysis, respectively. Pooled estimates were presented with a 95% confidence interval (CI). Summary estimates of the RRs/WMDs were derived using a fixed-effects model (Mantel-Haenszel method) or random-effects model (DerSimonian and Laird method).<sup>[12]</sup> Heterogeneity between studies was evaluated by  $I^2$  statistic. Publication bias was assessed by funnel plot, using Begg-Mazumdar indicator<sup>[13]</sup> and Harbord-Egger indicator.<sup>[14]</sup>  $P < 0.1$  indicated the presence of publication bias. For continuous data, if the study reported only the median and interquartile range (IQR) while sample size is larger than 100, then the median was regarded as mean and standard deviation (SD) was calculated as  $IQR/1.35$ .<sup>[15]</sup> All meta-analyses were performed using Review Manager (version 5.3; Cochrane Collaboration, Copenhagen, Denmark) and Stata

Software (version 12.0; Stata Corporation, College Station, TX, USA).

**RESULTS**

**Eligible studies and quality assessment**

A total of 13 studies involving 7056 patients were included in the final analysis.<sup>[7-10,16-24]</sup> Figure 1 presents the selection procedure. Table 1 describes the main details of the included studies. Methodological quality of the RCTs was adequate except blinding of endoscopist, as it could not be carried out in clinical practice [Figure 2].

**Cecal intubation rate**

A total of 13 studies were eligible for evaluation of the cecal intubation rate, which was almost identical for WE and AI (RR = 1.01, 95% CI = 0.99–1.02, *P* = 0.37, *I*<sup>2</sup> = 71%) [Table 2].

**Cecal intubation time**

A total of 13 studies were eligible for evaluation of mean cecal incubation time, which was demonstrated to be relatively longer in WE group (WMD = 1.57, 95% CI = 0.75–2.37, *P* = 0.002, *I*<sup>2</sup> = 98%) [Table 2].

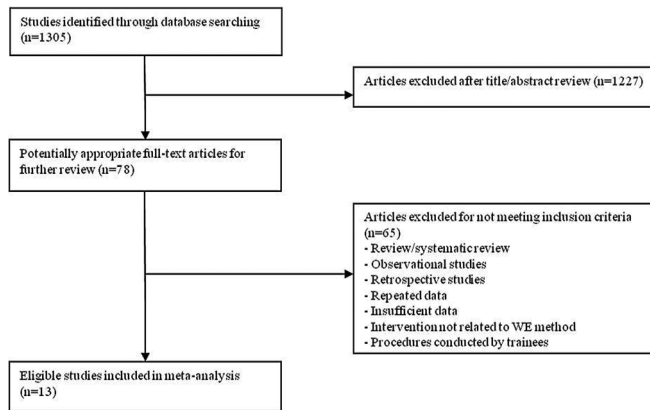


Figure 1: Flow diagram of the selection of trials

**Adenoma/polyp detection rate**

As for ADR, eight studies involving a total of 6067 colonoscopies were included, and in 1586 of them at least one adenoma was detected. ADR was significantly higher in WE group (RR = 1.28, 95% CI = 1.18–1.38, *P* < 0.00001, *I*<sup>2</sup> = 0%) [Table 2]. As for PDR, five studies involving a total of 3907 colonoscopies were included, and in 1768 of them at least one polyp was detected. Similarly, PDR was also higher in WE group (RR = 1.30, 95% CI = 1.21–1.39, *P* < 0.00001, *I*<sup>2</sup> = 0%) [Table 2].

**Pain score**

A total of nine studies investigating the difference in the maximum pain score during colonoscopy procedure were carried out using the visual analog scale from 0 to 10 to grade patients' pain (0 = no pain, 10 = most severe pain). Pooled estimates showed that the maximum pain score was significantly lower in WE group (WMD = -1.99, 95% CI = -2.68 to -1.30, *P* < 0.00001, *I*<sup>2</sup> = 94%) [Table 2].

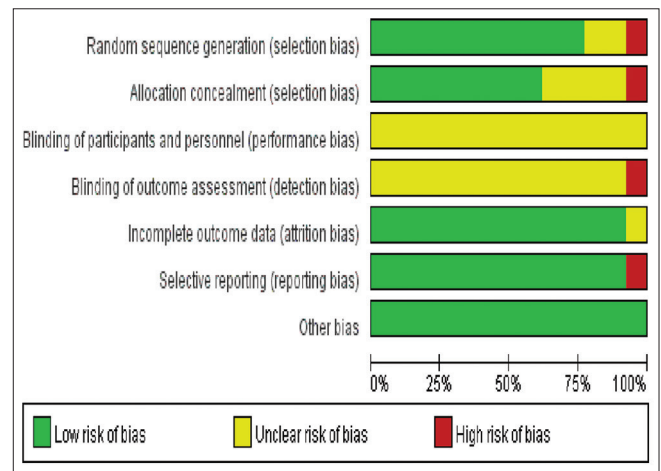


Figure 2: Summary of the risk of bias assessment

Table 1: Characteristics of the included studies

First author (year)	Country	Patients (n) water/air	Sedation mode	Water temp (°C)	Water volume (ml)	Cecal intubation time (min) water/air
Cadoni 2014	Italy	338/334	On-demand	37	550 (100-2000)	11.0±7.7/9.0±5.9
Cadoni 2015a	Italy	186/193	On-demand	37	475 (100-5100)	12.0±5.7/12.0±7.7
Cadoni 2015b	Italy/Czech	105/103	On-demand	37	600 (50-2650)	10.9±6.0/9.7±6.9
Cadoni 2017	Italy/Czech	408/408	On-demand	37	550 (350-800)	9.0±4.0/8.0±5.0
Falt 2015	Czech	46/46	On-demand	Room temp	447±127	7.6±2.7/7.4±3.4
Hsieh 2014	China	90/90	Minimal	Warm	1201±419	17.4±5.9/9.6±7.9
Hsieh 2017	China	217/217	Minimal/sedated	Warm	1224±521	14.0±6.3/7.5±5.0
Jia 2017	China	1653/1650	Unsedated/sedated	37	468±462	7.4±3.2/4.9±2.4
Leung JW 2013	USA	50/50	Unsedated	Warm	1652±712	13.0±6.7/12.0±7.0
Luo 2013	China	55/55	Unsedated	37	472±164	11.9±4.3/11.5±6.6
Ramirez 2011	USA	177/191	Minimal + on-demand	Room temp	UR	6.9±0.3/5.3±0.3
Wang 2015	China	100/100	On-demand	37	UR	8.2±1.1/7.0±1.4
Xu 2016	China	97/97	Unsedated	37	UR	6.9±1.3/10.6±2.5

UR: Unreported

**Table 2: Subgroup analysis of studies comparing water exchange with air insufflation for colonoscopy**

Outcome	Number of study	RR or WMD (95% CI)	P	I <sup>2</sup> (%)
Cecum intubation rate*	13	1.01 (0.99-1.02)	0.37	71
Cecum intubation time**	13	1.56 (0.75-2.37)	0.002	98
Adenoma detection rate*	8	1.28 (1.18-1.38)	<0.00001	0
Polyp detection rate*	5	1.30 (1.21-1.39)	<0.00001	0
Pain score**	9	-1.99 (-2.68-1.30)	<0.00001	94
On-demand sedation rate*	8	0.58 (0.44-0.77)	0.0002	64
Abdominal compression*	11	0.62 (0.51-0.74)	<0.00001	82
Reposition*	11	0.74 (0.63-0.86)	0.0001	68
Willingness to repeat the procedure*	9	1.14 (1.07-1.21)	<0.0001	90

\*ITT, \*\*PP. RR: Relative risk; WMD: Weight mean difference; CI: Confidence interval; ITT: Intention-to-treat; PP: Per-protocol

### On-demand sedation rate

A total of eight trials investigating on-demand sedation rate were eligible to assess if lesser sedation was required with WE (RR = 0.58, 95% CI = 0.44–0.77,  $P = 0.0002$ ,  $I^2 = 64\%$ ) [Table 2].

### Adjunct maneuvers

Pooled estimates of 11 trials showed that less abdominal compression (RR = 0.62, 95% CI = 0.51–0.74,  $P < 0.00001$ ,  $I^2 = 82\%$ ) and less reposition (RR = 0.74, 95% CI = 0.63–0.86,  $P = 0.0001$ ,  $I^2 = 68\%$ ) were needed during WE colonoscopy [Table 2].

### Willingness to repeat colonoscopy

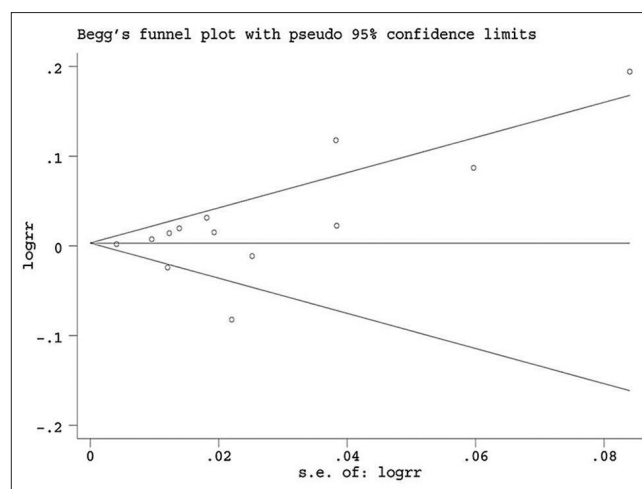
Pooled estimates of nine studies revealed that 91% of the patients (2499/2744) undergoing WE colonoscopy would repeat the procedure, when compared with 85% of those who (2330/2746) underwent AI colonoscopy (RR = 1.14, 95% CI = 1.07–1.21,  $P < 0.0001$ ,  $I^2 = 90\%$ ) [Table 2].

### Publication bias

Publication bias was evaluated by Begg's funnel plot and Egger's test. The shape of Begg's funnel plot did not reveal any evidence of asymmetry [Figure 3]. Egger's test did not suggest any evidence of publication bias ( $P = 0.30$ ).

## DISCUSSION

In this meta-analysis, although evidence was not adequate to prove that WE method was better for increasing cecal intubation rate, the use of WE seemed to have a higher ADR/PDR and patients' acceptance of colonoscopy. Moreover, pooled data showed that WE relieved patients' pain and minimized the need for on-demand sedation and

**Figure 3: Begg's funnel plot of publication bias test**

adjunct maneuvers. However, WE was demonstrated to be more time-consuming during the insertion phase.

ADR was considered to be the leading parameter of our study as the quality of endoscopist's performance of colonoscopy is mainly defined by the capacity of detecting precancerous lesions.<sup>[25]</sup> Currently, the recommended ADR target for a mixed male–female population is at least 25%.<sup>[26]</sup> However, previous studies have reported an approximately 22% adenoma missing rate undergoing tandem colonoscopy.<sup>[27]</sup> Interval cancers from these missed lesions would occur in 0.3% of the screened persons.<sup>[28]</sup> Thus, the recognition of interval cancers in patients with low ADR calls for meticulous examination. In our study, pooled data suggested that WE was superior to AI with respect to ADR (29.4% vs. 22.9%). The increase was significant (6.5%). Similar trend was observed for PDR (50.2% vs. 39.3%), with an increase of 10.9%. There are several possible mechanisms. The most important factor is the improved bowel preparation, which allows the colonoscopists focusing on searching for lesions. Besides, with water infusion, colon topography may not be changed and small polyps floating underwater can be more easily visible. Moreover, the magnifying effect of water can make the change in vasculature of neoplasm more obvious.

Minimizing pain and discomfort are of greatest importance for patients to accept colonoscopy. For this purpose, routine sedation, as one of the assistive techniques, has been commonly implemented into colonoscopy. However, with WE method, we found that there was a major reduction in pain score (by more than 1 unit compared with AI), thus the proportion of patients asking for sedation was significantly lower. Besides, our study also showed less need for abdominal compression or position change in WE group, since water reduces angulations during



intubation and facilitates instrument passage with less looping, especially in the left colon. All these contributed to a significantly higher proportion of patients willing to repeat the procedure with WE than AI (91% vs. 85%).

The time efficiency of performance is another important factor in adoption of a new method for colonoscopy. With regard to WE, more time has been spent for water infusion and suction during cecal intubation. In RCTs included in our study, the mean cecal insertion time for water method ranged from 6.9 to 17.4 min, suggesting a small but significant increase when compared with air method (4.9–12.0 min). However, the longer time (about 2 min) required by WE may play an important role in revealing more lesions during insertion, as confirmed in our study. We believe that this disadvantage might be overcome by more standardized technique training.

However, WE method has its own limitations. First, it is more prone to interference by suboptimal bowel preparation. Second, the prolonged insertion time will discourage its widespread application in current busy clinical practice. Third, it could not significantly improve an already high cecal intubation rate for most endoscopists at present. Fourth, it is more difficult for endoscopists to master this technique. However, it is noteworthy that there was no report of perforation or bleeding in patients undergoing WE colonoscopy examination. Severe procedure-related complications are not likely to be increased with WE method.

Several limitations of this study should be mentioned. First, significant heterogeneity was observed for some outcomes. The characteristics of study protocols, patient cohorts, endoscopists' experience, and other variabilities across studies may partly contribute to some heterogeneity within our analysis. Second, the blinding of outcome assessors was not possible for all variables. The lack of method concealment may contribute to a high Hawthorne effect which could not be completely ruled out and the final results might be affected to some extent. Third, raw data from some studies could not be compared directly. For example, pain score was not provided in the form of mean and SD in all studies.

## CONCLUSION

In summary, WE rather than AI during the insertion phase of colonoscopy could significantly lower maximum abdominal pain score and minimize the need for adjunct maneuvers, allow less sedative use without affecting the efficiency of the examination, and improve patients'

acceptance of the procedure. This novel technique should be considered as an option to reduce pain and discomfort in patients who prefer to undergo an unsedated colonoscopy, especially in those who have additional comorbidities with increased sedation risk. More importantly, it has shown to increase ADR/PDR in the colorectum. We postulate that the use of WE could assist colonoscopists with low ADR/PDR to improve their performance.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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