

Removal of infused water predominantly during insertion (water exchange) is consistently associated with an increase in adenoma detection rate - review of data in randomized controlled trials (RCTs) of water-related methods

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Abbreviations: ADR, adenoma detection rate; ANOVA, analysis of variance; BMI, body mass index; ITT, intent-to-treat; PEG, polyethylene glycol; RCT, randomized controlled trial; SD, standard deviation

Introduction: Variation in outcomes in RCTs comparing water-related methods and air insufflation raises challenging questions regarding the new approach. This report reviews impact of water exchange - simultaneous infusion and removal of infused water during insertion on adenoma detection rate (ADR) defined as proportion of patients with a least one adenoma of any size.

Methods: Medline (2008-2011) searches, abstract of 2011 Digestive Disease Week (DDW) meeting and personal communications were considered to identify RCTs that compared water-related methods and air insufflation to aid insertion of colonoscope.

Results: Since 2008, eleven reports of RCTs (6 published, 1 submitted and 4 abstracts, n=1728) described ADR in patients randomized to be examined by air and water-related methods. The water-related methods differed in timing of removal of the infused water - predominantly during insertion (water exchange) (n=825) or predominantly during withdrawal (water immersion) (n=903). Water immersion was associated with both increases and decreases in ADR compared to respective air method patients and the net overall change (-7%) was significant. On the other hand water exchange was associated with increases in ADR consistently and the net changes (overall, 8%; proximal overall, 11%; and proximal <10 mm, 12%) were all significant.

Conclusion: Comparative data generated the hypothesis that significantly larger increases in overall and proximal colon ADRs were associated with water exchange than water immersion or air insufflation during insertion. The hypothesis should be evaluated by RCTs to elucidate the mechanism of water exchange on adenoma detection.

Introduction

Several water-related methods identified by Medline searches were reviewed in 2008 to raise awareness of simple inexpensive colonoscopist-controlled maneuvers.¹ As adjuncts to air insufflation they eased passage through diverticular segments in the sigmoid colon, and sped arrival to the splenic flexure and cecum. Warm water was used to decrease spasms. These and subsequent observational reports were focused primarily on

reducing pain during colonoscopy. They have been dubbed air-water hybrids or more popularly known as water immersion due to endorsement by leading US experts. Early on concerns were expressed regarding the possible decrease in the ability to detect subtle mucosal lesions because of residual feces-contaminated water.² No remedial maneuvers had been proposed until a modern method of warm water infusion in lieu of air insufflation incorporating water exchange to remove the residual feces was described. The novel approach enabled 23 of 44 (52%) patients to complete unsedated colonoscopy using on-demand sedation in a cultural setting where sedation was standard.³

In these studies, polyp or lesion detection was described as not significantly different between the air insufflation and the water-related methods (**Table 1**)^{1,4,5} or average adenoma detection

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rate (ADR), defined as the proportion of patients with at least one adenoma of any size, was 48% (**Table 2**).^{3,6} In the first US observational study to assess the efficacy of the modern water method³ in scheduled, unsedated patients, an incidental finding of a trend towards a higher ADR was noted (**Table 3**).⁷ This prompted a retrospective review of observational data which suggested the hypothesis that the water method significantly increased ADR (**Table 3**).⁸ In the current follow up review of water-related methods, we assess the impact of water exchange during insertion (a unique component of the water method) on ADR. Reported RCTs⁹⁻¹⁴ and abstracts presented at 2011 DDW¹⁵⁻¹⁸ or full papers brought to the attention of FWL^{18,19} were included.²⁰ Aim is to address the question if water exchange deserves to be evaluated further in RCTs conducted by different investigators in diverse clinical settings.

Methods

We recently completed a review²⁰ of RCTs of water-related methods and air method published or presented since our prior review in 2008.¹ Comparative data indicated a greater attenuation of pain being associated with water exchange during insertion.²⁰ Comparison is now extended to ADR. The method section of each of the identified RCTs was evaluated by FWL to determine when the infused water was removed – predominantly during insertion or predominantly during withdrawal. When feasible the authors of these studies were contacted to obtain further details for consideration. Adenoma detection rates are grouped according to whether the infused water was removed predominantly during withdrawal^{9,11,13,14,18,19} or predominantly during insertion by water exchange.^{10,12,15-17} The difference between the air insufflation and the water-related method group in each report was calculated. The first draft of the review was distributed to all the co-authors. Appropriate modifications were incorporated into the final draft.

Results

Our review identified one submitted and six published reports and four abstracts of RCTs presented at 2011 Digestive Disease Week (DDW). They compared air insufflation versus water-related methods to aid insertion of the colonoscope. All eleven RCTs (n=1728) reported ADR. The section on methods in five published studies^{9-12,14} provided detailed description of the timing of removal of infused water; the authors in five other reports^{13,15-17,19} verified this information; and access to the full report for writing an editorial comment provided the needed information in the eleventh report.¹⁸ Studies can be divided broadly into two categories; the infused water was removed predominantly during insertion phase (water exchange, n=825) or during withdrawal phase (water immersion, n=903). The demographic and procedure-related variables were summarized in a previous review.²⁰ In each study randomization appeared to have distributed equivalent patients to the air and water groups evenly.²⁰ The ADR in the air insufflation and water-related method groups are summarized in **Tables 4** to **6**. Absence of water exchange was associated with both increases and decreases in ADR compared to air insufflation. **Table 4** shows the net change was a significant reduction in overall ADR (-7%).

Water exchange was associated with increases in ADR consistently compared to air insufflation. **Table 5** shows the net increase in overall ADR (8%) was significant; and so were the net increases in the proximal colon (proximal overall ADR, 11% and proximal <10 mm ADR, 12%) (**Table 5**).

Discussions

A population-based report demonstrated that colonoscopy failed to eliminate completely interval cancers after screening colonoscopy.²¹ In the proximal colon case-control studies revealed screening colonoscopy did not reduce cancer mortality^{22,23} or reduced it at best by ~50%.²⁴ Adenoma detection rate but not cecal intubation rate was an independent predictor of risk of interval colorectal cancer after screening colonoscopy.²⁵ Taken together focusing on maneuvers to enhance detection of proximal lesions with malignant potential is a prudent approach to improve the quality and outcome of screening colonoscopy.

The effects of modern approaches on modifying ADR or polyp detection rate have been conflicting. These include use of high-definition, wide-angle endoscope,^{26,27} dye-spray chromoendoscopy,²⁸⁻³⁰ withdrawal time >6 min,^{31,32} and trainee involvement.³³⁻³⁶ Narrow band imaging did not enhance ADR.³⁷ Amazingly monitoring and feedback could increase polyp detection³⁸ but whether this will translate into increase in ADR is unknown. The third eye retroscope consistently increased total number of adenomas detected in the proximal colon in unblinded studies,³⁹⁻⁴¹ but the impact on ADR was not described. Educational aids provided conflicting results on bowel cleanliness^{42,43} and the effect on ADR also was not described. Several studies confirmed that split-dose bowel preparation improved quality scores assessed by unbiased observers,^{44,45} but no information on ADR was presented. It is logical that an improved quality score permits a more accurate examination and possibly a higher ADR but reported data do not support the claim. For example, although bowel preparation score (Ottawa scale) could be improved by morning preparation for afternoon colonoscopy, the improved cleanliness did not alter overall polyp detection rate, adenomatous polyps or number of patients with adenomas.⁴⁶ In the right colon one split-dose study showed 2 L polyethylene glycol (PEG) + ascorbic acid (n=52) provided a significantly better bowel preparation score than PEG+bisacodyl (n=55) but not a significantly higher ADR.⁴⁷ Parenthetically another split-dose study of 2 L PEG + ascorbic acid reproduced the superior cleansing effect but showed no increase in polyp/malignancy detection rate.⁴⁸

Advances have been made in the understanding of importance of proximal diminutive lesions (adenomas or hyperplastic and serrated polyps). Proximal diminutive lesions can harbor high risk dysplasia.^{8,49,50} The recent proposal to re-evaluate proximal hyperplastic polyps as serrated polyps^{51,52} with malignant potential dramatizes the need to attend to these lesions.^{53,54}

The above considerations prompted us to review the current status of clinical research studies on water-related methods, especially the impact on ADR, both overall and in the proximal colon. The advent of water-related methods revealed significant attenuation of colonoscopy discomfort.²⁰ Water exchange in particular was associated with significantly greater reduction

Table 1. Reports of polyp detection in RCTs using water-related methods

Reference	Indications	Design/Sedation	Polyp or Lesion Detection Rate
Hamamoto et al ²	All comers without exclusions	RCT/ None n=259	Air 42/129 (32.6%) Water 39/130 (30.0%)
Brocchi et al ⁴	Diagnostic and surveillance	RCT/On-demand n=327	Air 23/164 (14.0%) Water 24/163 (14.7%)
Park et al ⁵	Diagnostic, screening and surveillance	RCT/None n=80	Air 9/39 (23.1%) Water 17/41 (41.5%)
		Combined	Air 74/332 (22.3%) vs water 80/334 (24.0%) (p=0.6462)
		Summary comment	No apparent difference between air and water-related methods.

RCT, randomized controlled trial; n, number of patients in the study.

Table 2. Reports of polyp detection in observational studies using the water method

Reference	Indications	Design/Sedation	Polyps Detection Rate
Leung et al ³	Screening and surveillance	OS/On-demand n=44	Sedated 7/21 (33.3%) Unsedated 12/23 (52.2%)
Leung et al ⁶	Screening or surveillance	OS/½ & full-dose n=75	Water, ½ dose 24/43 (55.8%) Water, full-dose 14/32 (43.8%)
		Summary comment	Overall polyp detection rate was 57/119 (48%).

OS, observational study; n, number of patients in the study.

Table 3. Reports of adenoma detection in an observational study and a retrospective review of the water method

Reference	Indications	Design/Sedation	Adenoma Detection Rate (ADR)
Leung et al ⁷	Diagnostic, screening and surveillance	OS/None n=125	Air 16/62 (25.8%) vs water 23/63 (36.5%) (p=0.2474)
Leung et al ⁸	Screening or surveillance	Review/Yes n=1178	Air 184/683 (26.9%) vs water 173/495 (34.9%) (p=0.0031)
		Combined	Air 200/745 (26.8%) vs water 196/558 (35.1%) (p=0.0015)
		Summary comment	The water method appeared to increase ADR significantly.

OS, observational study; n, number of patients in the study; ADR, adenoma detection rate.

Table 4. Absence of water exchange (water immersion) was associated with both increases and decreases in overall ADR and the net change was a significant reduction

Reference	Removal of infused water occurred predominantly during withdrawal		Difference in ADR (%)	p ^d	Split-dose ^e	
	Air n/N (ADR %)	Water n/N (ADR %)				
Hsieh et al ^{9a}	31/89 (35)	27/90 (36)	1	NS	No	
Hsieh et al ^{19a}	13/51 (26)	15/51 (29)	3	NS	No	
Leung et al ^{14a}	44/114 (39)	47/112 (42)	3	NS	No	
Radaelli et al ^{11b}	46/114 (40)	29/116 (25)	-15	0.013	No	
Ransibrahmanakul et al ^{13a}	10/31 (32)	9/31 (29)	-3	NS	No	
Pohl et al ^{18b}	15/58 (26) ^c	19/58 (33) ^c	7	NS	Yes	
	Combined	159/457 (35)	127/458 (28)	-7	0.023	
	Summary comment	Water immersion is associated with a significant net reduction in ADR compared with air insufflation.				

^aMinimal sedation; ^bOn-demand sedation; ^cRe-calculated based on intent-to-treat; ^dFisher's exact test; ^eSplit-dose bowel preparation was defined as ½ of bowel cleansing agent was consumed on the day before and the other half in the early morning of day of colonoscopy.

of pain during colonoscopy than water immersion.²⁰ However, caution was expressed that the view was less clear and the lumen was more difficult to find when water was infused,^{9,19,53-55} echoing the comments on the limitation of suboptimal bowel preparation in an earlier report.² Suctioning dirty water and replacing it with

clean water was deemed time-consuming.¹⁸ On the other hand, during the developmental stages of the water method, we learned (by trial-and-error) that simultaneous removal of the dirty water as clean water was infused to show the lumen during insertion (water exchange) solved the problem of impaired visibility.^{3,7,10,12}

Table 5. Water exchange was associated with increases in overall ADR consistently and the net change was significant

Reference	Removal of infused water occurred predominantly during insertion		Difference in ADR (%)	p ^d	Split-dose ^e
	Air n/N (ADR %)	Water n/N (ADR %)			
Leung et al ^{12,a}	9/40 (23)	15/42 (36)	13	0.2292	No
Leung et al ^{10,b}	18/50 (36)	20/50 (40)	3	0.8369	No
Ramirez et al ^{15,c}	88/191 (46)	101/177 (57)	11	0.037	No
Amato et al ^{16,a}	42/113 (37)	46/116 (39)	2	NS	No
Portocarrero et al ^{17,c}	2/12 (17)	6/11 (55)	38	0.057	No
Combined	159/406 (39)	188/396 (47)	8	0.0187	
Summary comment	Water exchange is associated with a significant net increase in ADR compared with air insufflation.				

^aUnsedated; ^bOn-demand sedation; ^cSedated; ^dFisher's exact test; ^eSplit-dose bowel preparation was defined as ½ of bowel cleansing agent was consumed on the day before and the other half in the early morning of day of colonoscopy.

Table 6. Water exchange significantly increased ADR (both overall and <10 mm) in the proximal colon

Reference	Removal of infused water occurred predominantly during insertion		Difference in ADR (%)	p ^d
	Air n/N (ADR)	Water n/N (ADR)		
Leung et al ^{12,a}				
Proximal overall ADR	3/40 (8%)	7/42 (17%)	9%	0.3134
Proximal <10 mm ADR	3/40 (8%)	7/42 (17%)	9%	0.3134
Leung et al ^{10,b}				
Proximal overall ADR	12/50 (24%)	20/50 (40%)	16%	0.1328
Proximal <10 mm ADR	10/50 (20%)	19/50 (38%)	18%	0.0769
Ramirez et al ^{15,c}				
Proximal overall ADR	67/191 (35%)	81/177 (46%)	11%	0.0432
Proximal <10 mm ADR	59/191 (31%)	74/177 (42%)	11%	0.0306
Combined				
Proximal overall ADR	82/281 (29%)	108/269 (40%)	11%	0.0072
Proximal <10 mm ADR	72/281 (25%)	100/269 (37%)	12%	0.0043
Summary comment	Water exchange is associated with a significant net increase in proximal ADR compared with air insufflation.			

^aUnsedated; ^bon-demand sedation; ^csedated; ^dFisher's exact test.

The well-defined goal to develop a novel method^{7,12} for use in scheduled, unsedated patients without any possibility of backup sedation,⁵⁶⁻⁵⁸ i.e. no minimal or on-demand sedation, motivated the meticulous process to perfect the least painful maneuvers. Incidentally, even in the air method group, to optimize successful cecal intubation, time was taken to ensure avoidable discomfort would not be precipitated by hasty insertion. The prolonged examination time in the air insufflation group (37 min) represented "best effort" but the failure rate of cecal intubation was still ~20%.¹² The mean insertion time in the water method group, seemingly prolonged (34 min), was not significantly longer than that in the air insufflation group, but enhanced cecal intubation rate to 98%.¹² In other reports when backup sedation was permissible, the insertion times were all of a lower order of magnitude, 5 to 10 min for experienced colonoscopists, and 10 to 15 min for trainees inclusive of water exchange.²⁰ Thus, unless an endoscopist is contemplating offering patients scheduled, unsedated colonoscopy the use of the water method with water exchange per se is not a source of "prolonged" insertion time to limit its use.⁵⁹ Water exchange appeared to have been utilized only in some but not in all of the RCTs identified in the current review. Serendipitously, the divergent practice²⁰ provides a unique

opportunity to determine if water exchange has an impact on ADR. In a previous review heterogeneity of the identified RCTs was noted.²⁰ There were wide variations in indications, primary outcomes, trainee involvement, use of split-dose bowel preparation or not and sedation mode, pain score and pain scales, number of enrolled patients, temperature and volume of water used.²⁰ Adenoma detection rate was one of several secondary outcome measures in all but one¹⁵ of the identified RCTs. These considerations limit the appropriateness of performing meta-analysis on the identified data at this time.

Importantly simultaneous removal of infused water during insertion has become an indispensable maneuver to minimize uncomfortable distension of the colon in the scheduled, unsedated patients when unlimited water volume was allowed.^{3,7,10,12} Not initially intended to be a critical endpoint, water exchange provided effective salvage cleansing in patients with suboptimal bowel preparation.^{3,7,10,12} A detailed description of the water exchange maneuver has been published this year.^{60,61} Nuances of the water method⁶⁰⁻⁶² warrant reiteration. Omission of air insufflation during insertion minimizes the risk of excessive elongation of the colon. Suction removal of the residual air minimizes angulations at the flexures and redundant segments and minimizes the risk

of loop formation. In a collapsed airless colon, infusion of water confirms the location of the lumen to facilitate advancement of the colonoscope. While the lumen-identification maneuvers are being implemented and colonoscope advanced, the infused water is removed by suction to minimize preventable distention. Coincidentally simultaneous infusion and suction removal of water create turbulence in the vicinity of the tip of the colonoscope. The turbulence facilitates suspension of the residual feces for suction removal. Water exchange during insertion in the collapsed colon is an efficient maneuver to provide salvage cleansing of the mucosa. As most of the infused water used to guide insertion is removed by the time cecal intubation is achieved there is minimal suction required during withdrawal to clear the lumen. We speculate that reduced use of suction during the withdrawal phase minimizes contraction of the colon or need for re-insufflation of air to maintain a distended lumen for inspection. Fewer suction-induced collapses of the lumen or contractions of the colon render the inspection focused on lesion detection. The colonoscopist is not distracted by the need to suction residual feces and water and can concentrate on inspection. The combination of these factors more than the salvage cleansing may have been instrumental in enhancing ADR, since improvement of bowel preparation quality scores by other approaches has not been associated with enhanced ADR consistently.⁴⁴⁻⁴⁸

While the water method was developed initially for managing non ADR-related outcomes, the enhanced ADR provided by strict adherence to air exclusion and use of water exchange deserves to be evaluated further. Comparative data appear to reveal that ADR varies depending on whether water exchange was used or not. Water exchange^{3,7,10,12} may be a critical component of the water method in favorably influencing ADR. The hypothesis should be evaluated by additional RCTs to generate the appropriate mix of RCTs for future meta-analysis. Testing of the hypothesis holds the promise of elucidating the mechanism of the water method on enhancing ADR.

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Disclosure

The authors have no conflict of interests to disclose relevant to this study.

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