

The water method significantly enhances proximal diminutive adenoma detection rate in unsedated patients

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Abbreviations: ADR, adenoma detection rate; SD, standard deviation; VAMC, Veterans Affairs Medical Center

Background: Colonoscopy has been reported to fail to prevent some post screening colonoscopy incident cancers or minimize cancer mortality in the proximal colon. These reports question the effectiveness of colonoscopy in detecting all proximal adenomas. Diminutive ones which can be obscured by residual feces are particularly at risk. The water method provides salvage cleansing of sub-optimal preparations.

Objective: To test the hypothesis that the water method enhances proximal diminutive adenoma detection rate (ADR).

Design: The data bases of two parallel RCT were combined and analyzed.

Setting: Two Veterans Affairs endoscopy units.

Patient and Methods: The water and air methods were compared in these two parallel RCT examining unsedated patients.

Main Outcome Measurements: The combined data on diminutive and overall ADR in the proximal colon, overall ADR, cecal intubation rate, withdrawal time and global bowel cleanliness score.

Results: Data in the water (n=92) and the air (n=90) groups were assessed. The water method yielded a significantly higher proximal diminutive ADR, 28.3% vs. 14.4% (p=0.0298); cecal intubation rate, 99% vs. 90% (p=0.0091); mean withdrawal time 19 (10) vs. 15 (8) min (p=0.0065) and mean global bowel cleanliness score during withdrawal, 2.6 (0.7) vs. 2.3 (0.6) (p=0.0032). Increase in proximal overall ADR in the water group approached significance, 29.3% vs. 16.7% (p=0.0592).

Limitation: Small number of predominantly male veterans.

Conclusion: The significantly higher cecal intubation rate, longer mean withdrawal time and better mean global bowel cleanliness score favor the outcome of significantly enhanced proximal diminutive ADR in the water group.

Introduction

Colonoscopy has been reported to fail to prevent some post screening colonoscopy incident cancers or minimize cancer mortality in the proximal colon^{1,2}. While the explanations are not fully available, these reports raise questions regarding the effectiveness of colonoscopy in detecting proximal adenomas which are presumptive precursors of cancers. Diminutive adenomas are particularly at risk of being obscured by residual feces. A water method to aid colonoscope insertion in unsedated patients involved warm water infusion in lieu of air insufflation, and suction removal of infused water and residual air to collapse the lumen to minimize discomfort³⁻⁸. A consecutive group observational study in a small number of unsedated patients revealed a numerically higher overall adenoma detection rate (ADR, proportion of patients with

at least one adenoma of any size) in the water group (36.5% of 62 vs. 25.8% of 63; p=0.2474)⁵. Salvage cleansing was observed with poor bowel preparation in the water and the air groups being 1 of 62 and 8 of 63 patients (p=0.0325), respectively⁵. A retrospective study of sedated patients provided confirmatory ADR data with significantly higher ADR in the water than in the air group (34.9% of 495 vs. 26.8% of 683; p=0.0031)⁶. The retrospective data, however, were limited because cecal intubation rate, withdrawal time and quality of bowel preparation were not included. In the context of improving quality of screening colonoscopy⁹ these observations generated the hypothesis that the water method has the potential to increase ADR during withdrawal in screening patients⁶. We recently completed two parallel RCT in veterans accepting scheduled unsedated colonoscopy⁷ or the option of sedation on demand⁸. The significant impact of the water method on the primary outcomes in terms of attenuating discomfort⁷ or enhancing completion of unsedated colonoscopy⁸, respectively, has been reported. Neither outcome is considered measures of quality. On the other hand ADR is both a measure of quality⁹ and an independent predictor of risk of post screening colonoscopy

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cancer¹⁰. In the current report, we conducted an assessment of the combined data bases of these two RCT to optimize the sample size of patients randomized to be examined by equivalent water and air methods. We searched for evidence to support the hypothesis that the water method enhances proximal diminutive adenoma detection rate (ADR) in unsedated patients.

Methods

The air method during insertion

Minimal air insufflation was used to aid colonoscope insertion. Colonoscope shortening maneuver, abdominal compression by the assistant and change of patient position were utilized as needed. Contact with residual feces which would smear the lens and impair the view was avoided. Cecal intubation was defined as passage of the colonoscope tip to a point proximal to the ileocecal valve so that the entire cecal caput, including the medial wall of the cecum between the ileocecal valve and appendix orifice was visible⁹.

The water method during insertion

Unlike water-related techniques used as adjuncts to air insufflation, unique features of the water method³⁻⁸ are as follows. Warm water (normal water, not saline) was infused in lieu of air insufflation as the “principal modality” to decrease colonoscopy discomfort. With the help of a peristaltic pump water at 37°C (maintained by a water bath) was infused through the biopsy channel. Removal of residual air reduced angulations at the flexures (e.g. sigmoid, splenic, hepatic and redundant segments) and collapsed the colon around the colonoscope. The colonoscope tip was oriented towards the “slit-like lumen” ahead. The infused water opened the lumen if the orientation was correct. Water infusion was stopped if the orientation was incorrect. The tip of the colonoscope was pulled away from the mucosa and redirected. The colonoscope was advanced by repeated insertion and withdrawal motions of the colonoscope with a torque in the direction of the expected lumen, and intermittent water infusion. Suspended residual feces obscuring the view were suctioned and replaced by clean water until the colonic lumen was visualized again. The volume of water needed to clear the view was unrestricted; up to 200 (clean colon) to 2000 (dirty colon) ml was necessary. Most of the infused water in fact was aspirated into the suction bottle instead of remaining in the colon. Over-distension could be obviated. The cleansing effect serendipitously optimized the colonic mucosa for inspection. Insufflated air could lengthen the colon and exaggerate angulations at the flexures making insertion in the unsedated patient difficult. The air pump was turned off to avoid “accidental” air insufflation during insertion. Minimization of angulations at the sigmoid flexure by suction removal of residual air was well-explained by Mizukami et al.¹¹. If advancement failed, the assistant would provide abdominal compression followed by the patient changing position if necessary. No abdominal pressure or change in patient position was employed if the advancement was uninterrupted. Cecal intubation was suggested in the early stage of development of the water method by appropriate movement of the endoscopic

image on the monitor screen when the right lower quadrant was palpated, or ~90 cm of the colonoscope in the short configuration was in the colon; and in the later stage, visualization of the appendix orifice under water. The cecum was then distended by air to confirm cecal intubation as defined above for the air method⁹.

In general there was not a lot of water leakage through the anus. We reported that “some patients did pass the water per anus as a bolus, requiring several large towels to soak up. We did not record the frequency of such occurrences, or survey the assistant specifically about the ‘mess’ created by such expulsions. We recorded assistant satisfaction after each colonoscopy. Despite an occasional ‘mess’ the responses significantly favored the water method.”⁷

Both methods during withdrawal

Air insufflation was used to distend the colon for inspection, biopsy and polypectomy. Washing of the stool covered mucosa and inspection behind folds were performed systematically. In the water group residual fluid around polyps was suctioned before polypectomy. Small polyps that dropped into nearby pool of fluid were retrieved by aspirating the fluid and polyps into the suction trap. After turn around in the rectum, residual air in the colon was removed by suction.

Study design

We searched the data bases of two recently reported RCT^{7,8}. They were designed to determine if the water method significantly improved non ADR-related primary outcomes in veterans accepting the option of scheduled unsedated (NCT00747084) or on demand (NCT00920751) sedation colonoscopy. Each RCT was approved by local Institutional Review Board (IRB) – the VA Greater Los Angeles (VAGLAHS) and the Northern California (VANCHCS) Healthcare Systems, respectively. All participants signed consent before participation.

At the Sepulveda Ambulatory Care Center, VAGLAHS (11/07-4/09) enrolled veterans undergoing unsedated colonoscopy were randomized to the water (n=42) or air (n=40) group⁷. At the Sacramento Veterans Affairs Medical Center, VANCHCS (4/09-10/09), enrolled veterans accepting on demand sedation colonoscopy were randomized to the water (n=50) or air (n=50) group⁸. The impact of the water method on the primary outcomes of discomfort⁷ or completion of unsedated colonoscopy⁸, respectively, has been described. For the current report, we searched the de-identified data bases of these two RCT tabulating proximal (proximal to the splenic flexure) diminutive and proximal overall ADR, overall ADR for the entire colon, cecal intubation rate, withdrawal time and global bowel cleanliness scores.

The data were evaluated using intent-to-treat analysis of outcomes related to the index colonoscopy. Group means (SD) were compared using Student’s t tests; and frequency counts (%), by Fisher’s exact test. Two ways analysis of variance (ANOVA) was performed to assess the impact of the endoscopists or method on proximal diminutive ADR in the subgroup of screening colonoscopy patients.

Results

The two groups showed no significant difference in mean age, gender distribution, body mass index and indications for colonoscopy (**Table 1**). Cecal intubation rate was significantly higher in the water group compared to the air group, 99% vs. 90% ($p=0.0091$, Fisher's exact test). Cecal intubation and total procedure times were comparable; mean withdrawal time was significantly longer in the water group than the air group, 19 (10) vs. 15 (8) min; ($p=0.0065$, Student's *t* test). Volume of water used was significantly lower in the air group.

The mean global bowel cleanliness scores during insertion were comparable between the air and water groups (**Table 2**). There was a significantly better mean global bowel cleanliness score in the water group than the air group during withdrawal, 2.6 (0.7) vs. 2.3 (0.6) ($p=0.0032$, Student's *t* test). The improvement in the water group was significant greater than that in the air group.

There was a significantly higher proximal diminutive (<10

mm) ADR in the water group (28.3%) compared to the air group (14.4%) ($p=0.0298$, Fisher's exact test). Overall proximal ADR was numerically higher in the water group (29.3%) compared to the air group (16.7%); and the difference approached significance ($p=0.0592$, Fisher's exact test). Overall ADR was numerically higher in the water group, 38% vs. 30% but the difference was not statistically significant ($p=0.2662$, Fisher's exact test). Distal diminutive and distal overall ADR were not significantly different (**Table 3**).

Trainees were not involved in the studies. Three staff endoscopists performed all the colonoscopies. At one site screening, surveillance and diagnostic and at the other site only screening and surveillance colonoscopies were randomized. To address possible variations in ADR based on endoscopists' experience, a further subgroup analysis was performed using only the patients who underwent screening colonoscopy (**Table 4**). The method ($p=0.0242$, two way ANOVA) but not the endoscopists or the interaction between the method and the

Table 1. Patient age, colonoscopy indications and procedure-related outcomes in the air and water method groups

	Air (n=90)	Water (n=92)	p
Age (years)	62.1 (8.7)	63.1 (8.7)	0.4175 ^a
Gender (male/female)	88/2	91/1	0.6188 ^b
Body mass index	30.4 (6.4)	29.4 (5.5)	0.2332 ^a
Screening	52 (58%)	45 (49%)	0.2390 ^b
Surveillance	29 (32%)	39 (42%)	0.1704 ^b
Diagnostic (FOBT, BRBPR, etc.)	9 (10%)	8 (9%)	0.8037 ^b
Other	1 (1.1%)	2 (2.2%)	1.0000 ^b
Cecal intubation rate	81 of 90 (90%)	91 of 92 (99%)	0.0091 ^b
Cecal intubation time (min)	21 (17), n=81	22 (15), n=91	0.6253 ^a
Withdrawal time (min)	15 (8), n=81	19 (10), n=91	0.0065 ^a
Total procedure time (min)	36 (20), n=81	41 (19), n=91	0.0966 ^a
Volume of water used (ml)	109 (220)	1526 (656)	0.0001 ^a

n, number of patients; FOBT, fecal occult blood test; BRBPR, bright red blood per rectum. Mean (SD) or frequency (%). ^aStudent's *t* test; ^bFisher's exact test.

Table 2. Global bowel cleanliness scores during insertion and withdrawal

	Air (n=90)	Water (n=92)	p ^a
Insertion	2.2 (0.7)	2.1 (0.6)	0.1537
Withdrawal	2.3 (0.6)	2.6 (0.7)	0.0032
Change (withdrawal – insertion)	0.07 (0.3)	0.5 (0.5)	0.0001

n, number of patients. Mean (SD). ^aStudent's *t* test. Global bowel cleanliness scores were defined as 4=excellent, no feces; 3=good, small amount of feces; 2=fair, moderate amount of feces; 1=poor, a lot of feces, including solid. The scores reflect the global impression of the colonoscopist during insertion and withdrawal.

Table 3. ADR outcomes in the air and water method groups

	Air (n=90)	Water (n=92)	p ^a
Proximal* (<10 mm) ADR	13 of 90 (14.4%)	26 of 92 (28.3%)	0.0298
Proximal* (>10 mm) ADR	2 of 90 (1.1%)	1 of 92 (1.0%)	0.6188
Overall Proximal* ADR	15 of 90 (16.7%)	27 of 92 (29.3%)	0.0592
Distal (<10 mm) ADR	6 of 90 (6.7%)	13 of 92 (14.1%)	0.1448
Distal (>10 mm) ADR	8 of 90 (8.9%)	4 of 92 (4.4%)	0.2466
Overall Distal ADR	14 of 90 (15.6%)	17 of 92 (18.5%)	0.6945
Overall ADR	27 of 90 (30%)	35 of 92 (38%)	0.2762

n, number of patients. ADR, adenoma detection rate defined as the proportion of patients with at least one adenoma of any size. Frequency (%). *Proximal to the splenic flexure. ^aFisher's exact test.

Table 4. Effect of method and endoscopists on proximal diminutive ADR in patients undergoing screening colonoscopy

Method	Endoscopist 1		Endoscopist 2		Endoscopist 3		Total	
	n	ADR	n	ADR	n	ADR	n	ADR
Water	17	17.6%	16	12.5%	12	33.3%	45	20.0%
Air	19	5.3%	16	6.2%	17	5.9%	52	5.8%
Total	36	11.1%	32	9.4%	29	17.2%	97	12.4%

n, number of screening colonoscopies per group. ADR, refers to proximal diminutive (<10 mm) adenoma detection rate in this Table. Two way analysis of variance revealed the method produced a significant effect ($p=0.0242$) whereas endoscopists ($p=0.4473$) and interaction between method and endoscopists ($p=0.4411$) did not.

Table 5. Recent published overall ADR in sedated patients

Method or subjects	ADR	Reference
Without trainee involvement	28%	15
Narrow band imaging	23%	16
Male non veterans	24.4%	17
High definition colonoscope	24.7%	18
Patients in Canada	25.5%	19
Patients in Israel	26%	20
Withdrawal time >6 min	28.3%	21
Three slow endoscopists after monitoring of ADR	28.9%	22
High definition colonoscope	28.8%	23
Morning colonoscopies	29.3%	24
Chromoendoscopy and standard colonoscope	33.6%	25
Chromoendoscopy and standard colonoscope	35.4%	26
White light and high definition colonoscope	41% to 57%	34
Narrow band imaging	51%	35
Chromoendoscopy and high definition colonoscope	55.5%	34

endoscopists was a significant factor in determining proximal diminutive ADR.

Discussions

This report demonstrates a significantly higher proximal diminutive ADR in predominantly unsedated patients examined by an insertion method distinct from usual air insufflation. An independent predictor of the risk of post screening colonoscopy cancer is ADR¹⁰. Colonoscopy has been reported to fail to completely eliminate some post screening colonoscopy incident cancers or reduce cancer mortality in the proximal colon^{1,2}. Even diminutive adenomas can harbor malignancy^{8,12-14}. Inadequate bowel preparation can result in a cancer or important adenoma, particularly diminutive ones, hidden from view by feces. These observations support the need to evaluate simple, inexpensive, easily available method(s) that can increase proximal diminutive ADR. In the current report, the significantly higher proximal diminutive ADR in the water (28.3%) compared to the air (14.4%) group suggests adoption of the water method to aid insertion possibly may lead to improved quality of colonoscopy in unsedated patients. Confirmation of the efficacy of the water method in sedated patients will provide a plausible remedy for the draw back of colonoscopy in dealing with post screening colonoscopy incident cancers and cancer mortality in the proximal colon.

The air method associated with failed cecal intubation because

of discomfort in the scheduled unsedated patients in specific, or incomplete visualization due to poor bowel preparation in general was less effective in detecting proximal diminutive adenomas⁷. The water method capable of enhancing cecal intubation by decreasing discomfort in the scheduled unsedated patient in specific, or salvage cleansing of the colon in general was more effective in detecting proximal diminutive adenomas⁷. Some of the sedation on demand patients (water group, 22% vs. air group, 46%, $p=0.011$) received sedation to achieve 100% cecal intubation⁸, dampening the full impact of the water method. Nonetheless, a significantly higher proximal diminutive ADR was observed in the water group.

The air group overall ADR of 30% (Table 3) is comparable to those in studies employing standard equipment and techniques in sedated patients¹⁵⁻²⁴ (Table 5). The water group overall ADR of 38% (Table 3) could possibly exceed those in studies employing chromoendoscopy and standard colonoscope in sedated patients^{25,26} (Table 5). The significantly longer withdrawal time in the water group is consistent with the association between prolonged withdrawal time and higher ADR²¹. The longer withdrawal time may also reflect more time spent in obtaining biopsy or polypectomy in the water group.

Adherence to suction removal of residual air and water exchange in the collapsed colonic lumen to clear the view likely optimized the soaking effect of water on residual feces adherent to mucosal surfaces. Residual feces were suspended in the luminal water by the turbulence set up by the simultaneous suction and infusion of water and readily removed during the insertion

phase. The global bowel cleanliness score was significantly improved during withdrawal. One study of split-dose preparation producing superior cleanliness scores reported significantly higher polyp detection rate in those scored as fair/good (27.3%) or good/excellent (24.6%) compared with those rated as poor/fair (12.2%)²⁷. Three studies of split-dose bowel preparation also reported better cleanliness although the impact on ADR was not addressed²⁸⁻³⁰. One report did show split-dose significantly enhanced detection of flat lesions³¹. Same day bowel preparation yielded superior^{31,32} or equivalent³³ bowel cleanliness compared with split-dose. To minimize bias in favor of the water method due to salvage cleansing in patients with suboptimal bowel preparation, split-dose or same day bowel preparation should be incorporated into future studies. The advent of modern endoscopic equipments has brought higher ADR with white light and high definition colonoscope³⁴, narrow band imaging³⁵ or chromoendoscopy and high definition colonoscope³⁴ (Table 5). The hypothesis that the water method can enhance proximal diminutive ADR when these modern equipments are used deserves to be tested.

In contrast to recent reports on evaluation of enhancement of ADR in sedated patients by new technologies^{16,18,23,34,35}, focus on the withdrawal phase^{10,21,22,25,26} and time of day²⁴ of colonoscopy or timing of bowel preparation³¹ and removal of polyps during insertion³⁶, we have described possible enhancement of proximal diminutive ADR on withdrawal in unsedated patients by the water method. Previous reports of worldwide availability of unsedated colonoscopy focused discussions on cecal intubation, patient tolerance, absence of sedation side-effects and potential cost savings³⁷. There is a paucity of information on ADR in unsedated patients; reported polyp detection rates ranged from 19%³⁸ and

20%³⁹ to 34%⁴⁰. Further evaluations of the impact of the water method on proximal diminutive ADR in the unsedated screening patients in diverse geographic and cultural settings are indicated. Similar comparisons in the sedated patients in the United States where sedation is the dominant practice may be worthwhile based on the results of a retrospective study⁶.

The strengths of this study are that the data are derived from the data bases of two parallel RCT comparing equivalent water and the air methods, and randomization has produced even distribution of demographic variables and indications for colonoscopy. The main limitation of this pilot report is the small number of predominantly male patients. The absence of blinding of the investigators (colonoscopist and assistant) is a drawback. In conclusion, the significantly higher cecal intubation rate, longer mean withdrawal time and better mean global bowel cleanliness score favor the outcome of significantly enhanced proximal diminutive ADR in the water group. Future studies extended to enroll larger numbers and subjects of both genders are warranted.

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Disclosure

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

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