

Removal of infused water predominantly during insertion (water exchange) is consistently associated with a greater reduction of pain score - review of randomized controlled trials (RCTs) of water method colonoscopy

Leung FW^{1,2}, Harker JO¹, Leung JW^{3,4}, Siao-Salera RM³, Mann SK^{3,4}, Ramirez FC⁵, Friedland S^{6,7}, Amato A⁸, Radaelli F⁸, Paggi S⁸, Terruzzi V⁸, Hsieh YH⁹

¹Sepulveda ACC, VAGLAHS, North Hill, CA; ²David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; ³Sacramento VAMC, VANCHCS, Mather, CA; ⁴UC Davis Medical Center, Sacramento, CA, USA; ⁵Mayo Clinic, Scottsdale, AZ, USA; ⁶Palo Alto VAMC, Palo Alto, CA; ⁷Stanford University, Palo Alto, CA, USA; ⁸Division of Gastroenterology, Valduce Hospital, Como, Italy; ⁹Buddhist Dalin Tzu Chi General Hospital, Chia-Yi, Taiwan

Key words: colonoscopy, water method, discomfort, pain, water exchange

Abbreviations: ANOVA, analysis of variance; BMI, body mass index; SD, standard deviation

Introduction: Variation in the outcomes in RCTs comparing water-related methods and air insufflation during the insertion phase of colonoscopy raises challenging questions regarding the approach. This report reviews the impact of water exchange on the variation in attenuation of pain during colonoscopy by water-related methods.

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

Results: Since 2008 nine published and one submitted RCTs and five abstracts of RCTs presented at the 2011 DDW have been identified. Thirteen RCTs (nine published, one submitted and one abstract, n=1850) described reduction of pain score during or after colonoscopy (eleven reported statistical significance); the remaining reports described lower doses of medication used, or lower proportion of patients experiencing severe pain in colonoscopy performed with water-related methods compared with air insufflation (Tables 1 and 2). The water-related methods notably differ in the timing of removal of the infused water - predominantly during insertion (water exchange) versus predominantly during withdrawal (water immersion). Use of water exchange was consistently associated with a greater attenuation of pain score in patients who did not receive full sedation (Table 3).

Conclusion: The comparative data reveal that a greater attenuation of pain was associated with water exchange than water immersion during insertion. The intriguing results should be subjected to further evaluation by additional RCTs to elucidate the mechanism of the pain-alleviating impact of the water method.

Introduction

Several water-related methods uncovered by Medline searches in 2008 were reviewed to raise awareness of these simple inexpensive colonoscopist-controlled maneuvers to improve colonoscopy outcome.¹ As adjuncts to air insufflation they eased passage through diverticular segments in the sigmoid colon,² and sped arrival to the splenic flexure³ and cecum.^{4,5} Warm water was used to decrease spasms and minimize discomfort.⁶ A modern method of warm water infusion in lieu of air insufflation enabled 52% of

patients to complete unsedated colonoscopy when they accepted the option of on-demand sedation.⁷ The review¹ concluded that the novel warm water infusion in lieu of air insufflation method⁷ uniquely increased tolerance of unsedated colonoscopy in a cultural setting where sedation had been the usual practice. The author proposed that randomized controlled trials (RCTs) comparing the novel method with the usual method of air insufflation in patients receiving routine sedation, sedation on-demand or no sedation deserve to be considered.¹ In response to the call,¹ there has been a plethora of RCTs using variations of the theme.⁸⁻²⁰ The diversity of investigators, sites and cultural settings brought forth fascinating advances in this novel but under-recognized approach. In this follow up review of water-related methods, we aim to assess the impact of water exchange versus water immersion on the variation in attenuation of pain during colonoscopy.

*Correspondence to: Felix W. Leung; Email: felix.leung@va.gov
Submitted: May/10/2011; Revised: May/29/2011; Accepted: Jun/03/2011
Previously published online: www.landesbioscience.com/journals/jig
DOI: 10.4161/jig.1.3.18510

Methods

Medline (2008 to 2011) searches, abstracts of the 2011 Digestive Disease Week (DDW), and personal communications were considered to identify RCTs that compared water-related methods and air insufflation to aid insertion of the colonoscope. In studies that did not report pain scores in detail, data related to dosages of sedation medications or proportion of patients experiencing severe pain were tabulated. Appropriate RCTs with data on pain score were selected for further assessment. In all except six of these RCTs, the pain scale in which 0=no pain, and 10=most severe or worst pain was used. Three used a scale of 0=no pain, and 100=most severe or worst pain,^{5,12,18} and three used 0=no pain, and 5=most severe or worst pain.^{8,20,21} In order to compare across studies, the pain scores in these six RCTs were recomputed to use the 0 to 10 scale. 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 appropriate, the authors of these studies were contacted to obtain further details for consideration. Mean (SD) or median [IQR] of pain scores are grouped according to whether the infused water was removed predominantly during insertion by water exchange or the infused water was removed predominantly during withdrawal. In each of the RCT with data on the pain scores in the air insufflation and the water-related method groups, the difference between the air insufflation and the water-related method groups was tabulated. The first draft of the review was distributed to all the co-authors (primarily accessible authors of the included published trials). Differences in interpretation were discussed by e-mail exchanges. Appropriate modifications were incorporated into the subsequent and the final draft.

Results

Our review identified nine published and one submitted RCTs and five abstracts of RCTs presented at the 2011 DDW, which compared air insufflation with water-related methods to aid insertion of the colonoscope. In twelve of these RCTs (n=1827) in patients who did not receive full dose sedation detailed pain scores are available (**Tables 1 and 2**). The section on methods in ten^{5,8-13,15,16,19} of these studies provided description of the timing of removal of infused water and the author in two^{14,18} verified this information. Access to the full report for writing an editorial comment provided the needed information in one report.¹⁹

Studies can broadly be divided into two categories; the infused water was removed predominantly during the insertion (water exchange) or during the withdrawal phase (water immersion). **Table 1** shows the demographic and procedure-related variables. In each of these studies, the randomization appeared to have distributed equivalent patients to each of the air and water groups evenly. The mean (SD) or median [IQR] pain score in the air insufflation and water-related method groups are shown in **Table 3**. A difference between the mean or median pain scores of the air and water-related method group can be established (**Table 3**). The remaining reports described lower doses of medication used,^{17,21} or lower proportion of patients experiencing severe

pain in colonoscopy²⁰ performed with water-related methods compared with air insufflation (**Table 2**). Use of water exchange was consistently associated with a greater attenuation of pain score in patients not receiving full dose sedation (**Table 3**). One of ten trials reported the use of split-dose bowel preparation; nine did not, and the other five did not describe whether split-dose bowel preparation was used or not (**Table 4A**).

Discussions

The fascination with development of methodologies to minimize patient discomfort following publication of the review of water-related methods for colonoscopy¹ is well-illustrated by the abundance of RCTs,⁸⁻²¹ observational studies,²²⁻²⁸ retrospective reports,²⁹⁻³² commentaries,³³⁻³⁸ hypothesis papers,³⁹⁻⁴¹ editorials,⁴²⁻⁴⁴ and reviews⁴⁵⁻⁴⁹ that ensue. Variation in the details of the water-related methods employed was understandable because all except the involved trainees were experienced colonoscopists well-trained in the air insufflation approach. Ingrained air insufflation-related maneuvers preferred by individual colonoscopist in speeding the completion of the examination were expected to be employed. The variation in outcomes in these RCTs, nonetheless, stimulated constructive comments regarding the consistency of the approach,^{9,10} why (besides lubrication and reduction of friction) a warm water-assisted method could diminish pain,⁵ the need for special technical endoscopic background for the approach to be really advantageous,¹² the appropriate temperature and amount of water to be infused.^{8,9} Insightful remarks were expressed over the leakage of water through the anus,⁸ the extra time needed for the water infusion,^{8,9} the lower utility in the hands of experts than trainees,⁸ the absence of an impact on colonoscopy pain in the hands of trainees⁸ and the need to consider an evaluation of water exchange.¹⁰ Legitimate frustrations were brought up that the view was less clear and the lumen was more difficult to find under water than with air insufflation, when the bowel preparation was suboptimal.^{8,9,19,32,34} These concerns echoed the limitation of poor bowel preparation pointed out earlier.⁴ Suctioning dirty water and replacing it with clean water was time-consuming.¹⁹ During the developmental stages of the water method, we learned (by trial-and-error) that the obvious and relatively simple maneuver of simultaneous suction-removal of the infused water during insertion (water exchange) provided the solution^{35,48} to an increasing number of these issues.

The explicit goal to develop a novel method^{15,22} for use in scheduled, unsedated patients without any possibility of back up sedation,⁵⁰⁻⁵³ i.e. no as-needed,³⁵ on-demand,³⁵ or minimal-sedation,³⁵ motivated the meticulous process to perfect the least painful maneuvers. Parenthetically if the pioneers who developed colonoscopy four decades ago had not been “distracted” by the use of sedation, we may not have to wait 40 years for the water method to be developed. Most importantly, removal of the infused water during insertion is an indispensable maneuver to minimize uncomfortable distension of the colon in the unsedated patient when unlimited volume of water is allowed;^{15,22} it is also an effective modality to salvage suboptimal bowel preparations;^{15,22} and cecal intubation in unsuccessful scheduled, unsedated patients examined by air insufflation.¹⁵

Table 1. Demographic and procedure-related variables in studies with detailed pain scores

Reference		M	F	Age	BMI	PAS	Cecal Intubation			Sites
							Success		Time	
							Final	ITT		
Brocchi et al. ⁵	Air	79	85	58	--	12	84%	84%	13	Italy
	Water	81	82	58	--	11	96%*	96%*	9**	
Park et al. ⁸	Air	20	19	52	24	--	90%	90%	8	Korea
	Water	20	21	56	25	--	95%	95%	10	
Hsieh et al. ⁹	Air	51	38	58	24	27	99%	99%	5	Taiwan
	Water	49	41	57	24	23	99%	99%	6**	
Hsieh et al. ¹⁰	Air	29	22	56	24	18	98%	98%	5	Taiwan
	Water	29	22	57	25	22	98%	98%	5	
	Water	29	22	52	24	21	98%	98%	6	
Leung et al. ¹¹	Air	114	0	63	29	29	100%	28%	15	United States
	Water	112	0	63	30	29	100%	51%†	10**	
Radaelli et al. ¹²	Air	66	48	59	25	34	96%	78%	5	Italy
	Water	68	48	58	25	37	94%	87%	7	
Ransibrahma-nakul et al. ¹⁴	Air	31	0	61	--	--	100%	94%	10	United States
	Water	30	1	61	--	--	100%	94%	11	
Pohl et al. ¹⁹	Air	42	16	62	--	--	96%	97%	6	Germany
	Water	43	15	63	--	--	100%	83%*	8**	
Leung et al. ¹³	Air	26	2	59	30	--	100%	100%	11	United States
	Water	25	3	60	31	--	100%	100%	9	
Leung et al. ¹⁵	Air	39	1	67	--	--	78%	78%	37	United States
	Water	40	2	66	--	--	98%*	98%*	34	
Leung et al. ¹⁶	Air	50	0	58	30	15	100%	54%	11	United States
	Water	49	1	61	30	13	100%	78%*	13**	
Amato et al. ¹⁸	Air	72	41	60	25	10	100%	71%	7	Italy
	Water	73	40	60	25	14	97%	87%	9	
Portocarrero et al. ²¹	Air	3	9	67	28	--	100%	100%	<16	United States
	Water	4	7	69	29	--	100%	100%	<14	

--, not reported; M=male, F=female; Age in years; BMI=body mass index; PAS=previous abdominal surgery; ITT, intent-to-treat; Cecum=success rate of cecal intubation; Insert time=insertion time in minutes; Water vol, water volume in ml; *vs. air, p<0.05, Chi Square test; **vs. air, p<0.05, t test or Mann-Whitney-U test; †OR 95% CI, 2.66 (1.48-4.79), p=0.0004, calculated using the Mantel-Haenszel method.

Table 2. Relevant demographic and procedure-related variables in reports without record of pain scores

Reference		M	F	n	Age	Cecum	Insert time	Severe pain	Mid/Fen	Site
Ramirez et al. ^{17,a}	Air	184	7	191	59	100%	5	--	3.1/77	United States
	Water	171	6	177	60	99%	7 ^b	--	2.8 ^b /69 ^b	
Sawant et al. ^{20,a}	Air	27	17	44	32	89% ^c	--	66%	--	India
	Water	25	19	44	34	93% ^c	--	30% ^d	--	
Portocarrero et al. ^{21,a}	Air	3	9	12	67	100%	<16	--	3.8/79	United States
	Water	4	7	11	69	100%	<16	--	1.4 ^b /59 ^b	

--, not reported; M=male, F=females; n, number; Cecum=success rate of cecal intubation; Insert time in minutes; ^aroom temperature water; ^bvs. air, p<0.05, t test; ^cCompleting colonoscopy without sedation; ^dvs. air, p<0.05, Chi Square test; Mid, Midazolam in mg; Fen, Fentanyl in mg.

A detailed description of the water exchange maneuvers was published this year.^{35,48} Meanwhile, water exchange appeared to have been utilized in only some^{13,15-18} but not in all^{6,8-12,14,19,20} of the RCTs identified in the current review. Serendipitously, this collection of RCTs provides a unique opportunity to determine whether water exchange has an impact on outcome, especially in providing attenuation of pain associated with colonoscopy without sedation.

While the cost of sedation – side-effects and patient burden

may be motivating factors to consider less sedation,⁴⁷ the increased efficiency for the colonoscopist, the diverse reimbursement incentives, and the absence of a consistently less painful approach favor the transition of current practice to deep sedation.^{35,46,54} Dr. Shapiro, former ASGE president and a supporter of unsedated colonoscopy lamented “The vast number of community colonoscopist gets by with discomfort by forming larger loops than are required for unsedated colonoscopy.”³⁷ Studies in which the options of scheduled, unsedated,^{8,15,20} on-demand,^{5,12,16,18,19}

Table 3. Reduction in pain score by the water-related techniques in patients who did not receive full dose sedation. Data are stratified according to timing of removal of the infused water – predominantly during withdrawal or insertion

Reference	Removal of infused water occurred predominantly during withdrawal					
	Air		Water		Pain score reduction	p
	n	Pain score	n	Pain score		
Brocchi et al. ^{5,a,d}	170	4.6 [1.8-9.2] ^f	170	2.9 [1.0-5.8] ^f	-1.7 ^f (37%)	0.001 [‡]
Park et al. ^{8,a,e}	39	2.6 (2.2) ^g	41	2.4 (2.2) ^g	-0.2 ^g (8%)	0.894
Hsieh et al. ^{9,b,e}	89	3.4 (2.8)	90	2.5 (2.5)	-0.9 (26%)	0.021 [*]
Hsieh et al. ^{10,b,e}	51	4.4 (2.6)	51	3.0 (2.2) ^h	-1.4 (32%)	0.004 [*]
			51	3.3 (2.4) ⁱ		
Leung et al. ^{11,b,e}	114	5.3 (2.7)	112	4.1 (2.7)	-1.2 (23%)	0.001 [*]
Radaelli et al. ^{12,c,d}	114	3.9 [1.4-5.4] ^f	116	2.8 [1.2-4.4] ^f	-1.1 ^f (28%)	0.001 [‡]
Ransibrahmanakul et al. ^{14,b,d}	31	4.8 (3.3)	31	3.1 (2.9)	-1.7 (35%)	<0.05 [*]
Pohl et al. ¹⁹	56	4.2 (2.3)	48	2.8 (1.9)	-1.3 (31%)	0.02
Reference	Removal of infused water occurred predominantly during insertion					
	Air		Water		Pain score reduction	p
	n	Pain score	n	Pain score		
Leung et al. ^{13,b,e}	28	4.1 (3.4)	28	1.3 (1.8)	-2.8 (68%)	0.0002 [*]
Leung et al. ^{15,a,d}	40	6 [--]	42	3 [--]	-3 (50%)	0.004 [‡]
Leung et al. ^{16,c,e}	50	4.9 (2.0)	50	2.3 (1.7)	-2.6 (53%)	0.0012 [‡]
Amato et al. ^{18,c,d}	113	4.9 [3.0-7.0] ^f	113	2.4 [1.0-5.0] ^f	-2.5 ^f (51%)	0.0001 [‡]

--, not reported; IQR, interquartile range; ^aunsedated; ^bminimal sedation for pre-medication; ^con-demand sedation; ^dmedian score [IQR]; ^emean score (SD); ^fConverted from 0 to 100 scale to 0 to 10 scale for comparability of pain measures; ^gConverted from 0 to 5 scale to 0 to 10 scale for comparability of pain measures; ^hLimited volume water infusion in the recto-sigmoid colon only; ⁱLarge volume water infusion throughout entire colon during insertion; *t test; ‡rank sum or Mann-Whitney U.

Table 4A. Heterogeneity in the design of the RCT comparing pain scores in patients examined by the air and the water-related methods – indications, primary outcome, trainee involvement and use of split-dose bowel preparation or not

Reference	Indications	Primary Outcome	Trainee	Split-dose bowel preparation ^a
Brocchi et al. ⁵	Scr, Sur, Dx	Percentages of complete colonoscopy	No	No
Park et al. ⁸	Sur, Dx	Colonoscopic success rate in 15 min	All	--
Hsieh et al. ⁹	Sur, Dx	Patient pain	No	No
Hsieh et al. ¹⁰	Sur, Dx	Patient pain	No	No
Leung et al. ¹¹	Scr, Sur, Dx	Completing minimal sedation	In part	No
Radaelli et al. ¹²	Scr, Sur, Dx	Need on-demand sedation	No	--
Ransibrahma-nakul et al. ¹⁴	Scr, Sur	Patient pain	All	No
Leung et al. ¹³	Scr, Sur	Patient pain	No	No
Leung et al. ¹⁵	Scr, Sur, Dx	Completing unsedated	No	No
Leung et al. ¹⁶	Scr, Sur	Completing unsedated	No	No
Amato et al. ¹⁸	Scr, Sur, Dx	Need on-demand sedation	No	--
Pohl et al. ¹⁹	Scr, Sur, Dx	Completing unsedated	No	Yes
Ramirez et al. ¹⁷	Scr	Adenoma detection rate	No	No
Sawant et al. ²⁰	Dx	Completing unsedated	All	--
Portocarrero et al. ²¹	--	Sedation requirement	No	--

--, not reported; Scr, screening; Sur, surveillance; Dx, diagnostic; ^aSplit 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.

minimal^{9-11,13,14} or full^{17,21} sedation were employed are included in this review. All except two^{8,21} of the RCTs with detailed data on pain score showed a significant impact of the use of water to aid insertion of the colonoscope, i.e., a significant reduction in mean or median pain score (**Table 3**). Even in one study⁸ in which no significant reduction was demonstrated; the pain score in the water-related method group was numerically lower. In another the patients received full sedation; and patients in the water method group did require less additional sedation medication.²¹

Other significant effects were manifested as less additional medications required after minimal^{11,13,14} or full-dose^{17,21} pre-medication, a lower proportion of unsedated patients who reported severe pain,^{15,20} or a higher proportion of patients who were able to complete colonoscopy without sedation when the on-demand sedation option^{16,18,19} or scheduled, unsedated option¹⁵ was employed. Compared with water immersion, water exchange produced a greater average reduction of pain score (- 56% versus - 27%) (**Table 3**).

Table 4B. Heterogeneity in the design of the RCT comparing pain scores in patients examined by the air and the water-related methods – sedation mode, pain score and pain scale, number of enrolled patients, temperature and volume of water used

References	Sedation Mode	Pain		Air		Water	
		score	Scale	n	n	Temp	Volume (ml)
Brocchi et al. ⁵	On-demand	Median	0-100	170	170	42°C	300 ^a
Park et al. ⁸	Unsedated	Mean	0-5	39	41	36°C	200 ^a
Hsieh et al. ⁹	Minimal	Mean	0-10	89	90	Room	322±81 ^b
Hsieh et al. ¹⁰	Minimal	Mean	0-10	51	51	Room	399±197 ^b
					51	Room	629±226 ^b
Leung et al. ¹¹	Minimal	Mean	0-10	114	112	Warm	>300 ^a
Radaelli et al. ¹²	On-demand	Median	0-100	114	116	37°C	>210 ^a
Ransibrahmanakul et al. ¹⁴	Minimal	Mean	0-10	31	31	37°C	1006±429 ^b
Leung et al. ¹³	Minimal	Mean	0-10	28	28	37°C	938
Leung et al. ¹⁵	Unsedated	Median	0-10	40	42	37°C	1767±651 ^b
Leung et al. ¹⁶	On-demand	Mean	0-10	50	50	37°C	1323±593 ^b
Amato et al. ¹⁸	On-demand	Median	0-100	113	113	37°C	--
Pohl et al. ¹⁹	On-demand	Mean	0-10	58	58	37°C	755±197 ^b
Ramirez et al. ¹⁷	Sedated	--	--			Room	--
Sawant et al. ²⁰	Unsedated	--	0-5	32	34	--	--
Portocarrero et al. ²¹	Sedated	Mean	0-5	12	11	Room	--

--, not reported; Sedated=full dose sedation medications given before start of colonoscopy; ^aMaximum volume infused; ^bMean±SD.

In the published RCT involving scheduled, unsedated patients, the water method was superior in terms of minimizing patient discomfort.¹⁵ In addition to the proof-of-principle observation related to the primary outcome the study reveals several unique features of colonoscopy discomfort in the unsedated patients. The data confirm reports of no correlation between total colonoscopy duration and maximum discomfort (reported during colonoscopy) or overall discomfort (reported after colonoscopy);⁵⁵ overall discomfort is uniformly lower than maximum discomfort,⁵⁵ these 2 measures are significantly correlated,⁵⁵ and the proportion with severe overall discomfort was significantly lower in the water group.⁴ The reduction of overall discomfort, previously non-significant,⁴ approaches significance. The significant decrease in maximum discomfort by the water method is new. Of interest was that the water method provided “salvage” cecal intubation in three subjects (re-examined at a later date) after failure due to the discomfort associated with the air insufflation method.¹⁵ The air insufflation method with sedation did not alter the failed outcome in the one subject caused by obstruction in the water method group.¹⁵

Decades of experience has clearly demonstrated that in the fully sedated patients, the reduction of patient discomfort by the water-related methods is of low relevance. The concern that suctioning dirty water and replacing it with clean water is time-consuming¹⁹ is a legitimate one. The prolonged insertion time of the water method in the scheduled, unsedated patients²² was deemed a major limitation to its widespread application;⁴² even the added time needed to learn the water method makes it impractical when only 30 min is allotted for each colonoscopy in practice. The mean insertion time ranging from 5 min to 13 min (Tables 1 and 2), however, attest to the feasibility of the methodological approach in practice settings besides that for the scheduled, unsedated patients. Nevertheless, others are satisfied with⁵⁶⁻⁵⁹ or still debating over⁵⁸ the use of water-related methods

as adjuncts to air insufflation.¹ Since all of the colonoscopists were trained in the air insufflation method the intent-to-treat failures in the water-related methods did not preclude completion of the colonoscopy when the colonoscopists switched back to the air insufflation method.^{12,17-19} Other incentives may be necessary for the water-related methods to be considered.

This review is a collection of RCTs reported by unblinded investigators with variable preference for air insufflation, colonoscopy expertise and experiences practicing in different cultural settings likely with unequal values and patients with varied thresholds of perception for pain and discomfort. Regardless of how the water is delivered and retrieved, temperature (room temperature to 42°C) or volume (200 to 2000 ml) of the water, the uniformity of the results (except for one involving trainees and another, fully sedated patients) that the water-related methods reduce pain compared with air insufflation is compelling. Because the included trials cover multiple US and non US sites (Tables 1 and 2), the result appears to be quite reproducible across diverse cultural and practice settings. These RCTs are testimonials of the collective efforts of investigators dedicated to developing a more tolerable colonoscopy for patients who do not or may not want to receive sedation.⁴⁵⁻⁵⁴ Documentation of procedural difficulties and the subsequent ways to resolve them has promoted progress in this important area of clinical investigation.

Table 4A and 4B show the heterogeneity of the identified RCTs. There are wide variations in indications, primary outcomes, trainee involvement, and use of split-dose bowel preparation or not (Table 4A) and sedation mode, pain score, pain scales, number of enrolled patients, temperature and volume of water used (Table 4B). Pain during colonoscopy is the primary outcome in only four of the RCTs. These considerations limit the appropriateness of performing meta-analysis on the identified data at this time. Furthermore, there did not appear to be a correlation between the volume of water used (Table 4B) and whether split-dose bowel

preparation was employed or not (**Table 4A**).

This review also illustrates an unexpected recognition of the ineffectiveness of original publications in the medical literature in providing accurate communication of all of the nuances of the practical components of a novel procedure. The initial review¹ and the associated observational reports^{7,22,23} and RCTs^{13,15,16} failed to communicate accurately the implementation of the maneuvers of water exchange. In the most recent RCT reported by Hsieh and co-workers¹⁰ a large and a limited volume of water were compared in the absence of removal of the infused water during insertion, i.e. no water exchange. The higher pain score in the large volume group (**Table 3**) further illustrated the importance of water exchange during insertion. Anecdotally, when infused water was not adequately removed during insertion, patients tend to report increased pain or strain to discharge water from the colon when air insufflation was initiated upon cecal intubation (personal communication, Drs. JW Leung and SK Mann, June 2011), consistent with the concern of water leakage via the anus raised by others.⁸ These observations may reflect the fixed volume of distension permissible by the colon and filling the colon partially by the un-removed water restricts the volume of air that could be infused comfortably. The insightful comments of the editors who commissioned the invited review⁴⁸ specifically requested tabulation and illustrations of the procedural details after assessment of the first draft of the submission (personal communication, Drs. Thomas Rösch & Jacques Bergman, Feb 2, 2011). A similar request was made by editors of an invited review⁴⁹ (personal communication, Dr. Sun-Young Lee, June 16, 2011) and an invited editorial⁶⁰ (personal communication, Dr. C. Mel Wilcox, August 21, 2011). Whether these advances in written presentation will bring about improved understanding on the part of other colonoscopists remains to be observed and documented.

The concerted effort in developing a comfortable method in the unsedated patients is laudable. The comparative data appear to reveal that the greater efficacy in attenuation of pain in patients not receiving full dose sedation is associated with water exchange during insertion. The evidence suggests that “water exchange”¹⁵ may be a critical component of water-related methods in minimizing pain during colonoscopy. The intriguing results should be subjected to further evaluation by additional RCTs to generate sufficient data for future meta-analysis. Testing of the hypothesis holds the promise of elucidating the mechanism of the pain-alleviating impact of the water method. Finally, we seem to have arrived at a similar conclusion as in the last review¹ - confirmation of the efficacy of the use of water exchange leading to its application in subgroups of patients examined with or without sedation would have potentially significant impact on enhancing colonoscopy outcome.

Acknowledgement

The study is supported in part by Veterans Affairs Medical Research Funds at Veterans Affairs Greater Los Angeles Healthcare System and an American College of Gastroenterology Clinical Research Award (FWL).

Disclosure

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

References

1. Leung FW. Water-related method for performance of colonoscopy. *Dig Dis Sci* 2008; 53:2847-50.
2. Falchuk ZM, Griffin PH. A technique to facilitate colonoscopy in areas of severe diverticular disease. *N Eng J Med* 1984; 310:598.
3. Baumann UA. Water intubation of the sigmoid colon: water instillation speeds up left-sided colonoscopy. *Endoscopy* 1999; 31:314-7.
4. Hamamoto N, Nakanishi Y, Morimoto N, Inoue H, Tatukawa M, Nakata S, et al. A new water instillation method for colonoscopy without sedation as performed by endoscopists-in-training. *Gastrointest Endosc* 2002; 56:825-8.
5. Brocchi E, Pezzilli R, Tomassetti P, Campana D, Morselli-Labate AM, Corinaldesi R. Warm water or oil-assisted colonoscopy: toward simpler examinations? *Am J Gastroenterol* 2008; 103:581-7.
6. Church JM. Warm water irrigation for dealing with spasm during colonoscopy: simple, inexpensive, and effective. *Gastrointest Endosc* 2002; 56:672-4.
7. Leung JW, Mann S, Leung FW. Option for screening colonoscopy without sedation - a pilot study in United States veterans. *Aliment Pharmacol Ther* 2007; 26:627-31.
8. Park SC, Keum B, Kim ES, Jung ES, Lee SD, Park S, et al. Usefulness of warm water and oil assistance in colonoscopy by trainees. *Dig Dis Sci* 2010; 55:2940-4.
9. Hsieh YH, Lin HJ, Tseng KC. Limited water infusion decreases pain during minimally sedated colonoscopy. *World J Gastroenterol* 2011; 17:2236-40.
10. Hsieh YH, Tseng KC, Hsieh JJ, Tseng CW, Hung TH, Leung FW. Feasibility of colonoscopy with water infusion in minimally sedated patients in an Asian community setting. *J Interv Gastroenterol* 2011, in press.
11. Leung CW, Kaltenbach T, Soetikno R, Wu KK, Leung FW, Friedland S. Colonoscopy insertion technique using water immersion versus standard technique: a randomized trial showing promise for minimal-sedation colonoscopy. *Endoscopy* 2010; 42:557-63.
12. Radaelli F, Paggi S, Amato A, Terruzzi V. Warm water infusion versus air insufflation for unsedated colonoscopy: a randomized, controlled trial. *Gastrointest Endosc* 2010; 72:701-9.
13. Leung JW, Mann SK, Siao-Salera R, Ransibrahmanakul K, Lim B, Cabrera H, et al. A randomized, controlled comparison of warm water infusion in lieu of air insufflation versus air insufflation for aiding colonoscopy insertion in sedated patients undergoing colorectal cancer screening and surveillance. *Gastrointest Endosc* 2009; 70:505-10.
14. Ransibrahmanakul K, Leung JW, Mann SK, Siao-Salera R, Lim BS, Hasyagar C, et al. Comparative effectiveness of water vs. air methods in minimal sedation colonoscopy performed by supervised trainees in the US - randomized controlled trial. *Am J Clin Med* 2010; 7:113-8.
15. Leung FW, Harker JO, Jackson G, Okamoto KE, Behbahani OM, Jamgotchian NJ, et al. A proof-of-principle, prospective, randomized, controlled trial demonstrating improved outcomes in scheduled unsedated colonoscopy by the water method. *Gastrointest Endosc* 2010; 72:693-700.
16. Leung JW, Mann SK, Siao-Salera RM, Ransibrahmanakul K, Lim BS, Canete W, et al. A randomized, controlled trial to confirm the beneficial effects of the water method on U.S. veterans undergoing colonoscopy with the option of on-demand sedation. *Gastrointest Endosc* 2011; 73:103-10.
17. Ramirez FC, Leung FW. The water method is associated with higher adenoma detection rate (ADR) - a head-to-head comparative study. *DDW 2011 abstract 601 and 601r*, program p. 301 and p. 435.
18. Amato A, Radaelli F, Paggi S, Spinzi G, Terruzzi V. Carbon dioxide insufflation (CO2) and warm water infusion (WWI) versus standard air insufflation (AI): preliminary results of a randomized controlled trial in unsedated colonoscopy. *DDW 2011 abstract 602*, program p. 301.
19. Pohl J, Messer I, Behrens A, Kaiser G, Mayer G, Ell C. Water infusion for cecal intubation increases patient tolerance, but does not improve intubation of unsedated colonoscopies. *Clin Gastroenterol Hepatol* 2011; in press.
20. Sawant PD, Samarth A, Vashishtha C, Patel J, Agasti A. Water infusion vs. air insufflation colonoscopy in unsedated patients - impact on patient discomfort. *DDW 2011 Poster Tu1434*, program p. 873.
21. Portocarrero DJ, Che K, Olafsson S, Walter MH, Sahba B, Jackson CS, et al. Application of the water method to aid colonoscope insertion in community settings in the United States is feasible: sedation requirement can be minimized without compromising patient-centered and procedure-related outcomes. *DDW 2011 Poster Tu1430*, program p. 873.
22. Leung FW, Aharonian HS, Leung JW, Guth PH, Jackson G. Impact of a novel water method on scheduled unsedated colonoscopy in U.S. veterans. *Gastrointest Endosc* 2009; 69:546-50.
23. Leung JW, Salera R, Toomsen L, Mann S, Leung FW. Pilot feasibility study of the method of water infusion without air insufflation in sedated colonoscopy. *Dig Dis Sci* 2009; 54:1997-2001.
24. Frossard JL, Gervaz P, Huber O. Water-immersion sigmoidoscopy to treat acute GI bleeding in the perioperative period after surgical colorectal anastomosis. *Gastrointest Endosc* 2010; 71:167-70.
25. Leung FW, Mann SK, Leung JW, Siao-Salera RM, Jackson G. The water method is effective in difficult colonoscopy - it enhances cecal intubation in unsedated patients

- with a history of abdominal surgery. *J Interv Gastroenterol* 2011, in press.
26. Leung JW, Ransibrahmanakul K, Toomsen L, Mann SK, Siao-Salera RM, Leung FW. The water method combined with chromoendoscopy enhances adenoma detection. *J Interv Gastroenterol* 2011; 1:53-8.
 27. Ramirez FC, Leung FW. Adopting the water method: lessons, tips and pitfalls learned. *Am J Clin Med* 2010; 7:121-3.
 28. Ramirez FC, Leung FW. The water method for aiding colonoscope insertion: the learning curve of an experienced colonoscopist. *J Interv Gastroenterol* 2011; 1:97-101.
 29. Leung JW, Mann SK, Do L, Siao-Salera R, Leung FW. More polyps are seen on screening colonoscopy with water infusion in lieu of air insufflation (water method) compared with usual air insufflation. *Am J Clin Med* 2010; 7:137-9.
 30. Leung FW. Patient time burden and sedation-related complications in screening and surveillance colonoscopy. *Am J Clin Med* 2010; 7:109-12.
 31. Leung FW, Leung JW, Siao-Salera RM, Mann SK. The water method significantly enhances proximal diminutive adenoma detection rate in unsedated patients. *J Interv Gastroenterol* 2011; 1:8-13.
 32. Leung FW, Leung JW, Siao-Salera RM, Mann SK, Guy Jackson G. The water method significantly enhances detection of diminutive lesions (adenoma and hyperplastic polyp combined) in the proximal colon in screening colonoscopy - data derived from two RCT in US veterans. *J Interv Gastroenterol* 2011; 1:48-52.
 33. Rex DK. Water infusion vs. air insufflation during colonoscopy. *J Watch Gastroenterol* October 2, 2009.
 34. Friedland S. The water immersion technique for colonoscopy insertion. *Gastroenterol Hepatol (N Y)* 2010; 6:555-6.
 35. Leung FW. Is there a place for sedationless colonoscopy? *J Interv Gastroenterol* 2011; 1:19-22.
 36. Siao-Salera R, Leung JW, Mann SK, Canete W, Gutierrez R, Galzote CR, et al. Options of sedation or no sedation for colonoscopy - the perspective of the GI nurses and technicians. *J Interv Gastroenterol* 2011; 1:37-41.
 37. Leung FW. Patients' perspective - written testimonials from physician-patients and oral accounts presented by patients in person. *J Interv Gastroenterol* 2011; 1:40-6.
 38. Friedland S, Leung FW. Learning and teaching the water method (with videos). *J Interv Gastroenterol* 2011, 1:132-4.
 39. Granados-Savatgy L, Bradham DD, Blohm L, Siao-Salera R, Leung JW, Leung FW. Cost benefit analysis and cost estimating: sedated vs. unsedated colonoscopy at one VAMC. *Am J Clin Med* 2010; 7:147-50.
 40. Leung JW, Do L, Siao-Salera RM, Parikh DA, Mann SK, Leung FW. Retrospective data showing the water method increased adenoma detection rate - a hypothesis generating observation. *J Interv Gastroenterol* 2011; 1:3-7.
 41. Leung, FW. A hypothesis-generating review of the water method for difficult colonoscopy. *Scand J Gastroenterol* 2011; 46:517-21.
 42. Wasan SK, Schroy PC. Water-assisted unsedated colonoscopy: does the end justify the means? *Gastrointest Endosc* 2009; 69:551-3.
 43. Davila ML, Davila RE. The demise of air insufflation and the rise of the warm water infusion method. *Gastrointest Endosc* 2009; 70:511-4.
 44. Robbins DH. Unsedated colonoscopy: just add water? *Gastrointest Endosc* 2010; 72:710-1.
 45. Leung FW, Aljebreen AM, Brocchi E, Chang EB, Liao WC, Mizukami T, et al. Sedation-risk-free colonoscopy for minimizing the burden of colorectal cancer screening. *World J Gastrointest Endosc* 2010; 2:81-9.
 46. Leung FW, Aljebreen AM. Unsedated colonoscopy: Is it feasible? *Saudi J Gastroenterol* 2011; 17:289-92.
 47. Leung FW, Leung JW, Mann SK, Friedland S, Ramirez FC, Olafsson S. DDW 2011 cutting edge colonoscopy techniques - state of the art lecture master class - warm water infusion/CO2 insufflation for colonoscopy. *J Interv Gastroenterol* 2011; 1:78-82.
 48. Leung FW, Leung JW, Mann SK, Friedland S, Ramirez FC. The water method significantly enhances patient-centered outcomes in sedated and unsedated colonoscopy. *Endoscopy* 2011; May 24. [Epub ahead of print]
 49. Leung FW. Unsedated colonoscopy and the water method for minimizing discomfort in the unsedated patients. *Intest Res* 2011, in press.
 50. Leung FW, Aharonian HS, Guth PH, Chu SK, Nguyen BD, Simpson P. Involvement of trainees in routine unsedated colonoscopy: review of a pilot experience. *Gastrointest Endosc* 2008; 67:718-22.
 51. Leung FW. Unsedated colonoscopy introduced as a routine option to ensure access is acceptable to a subgroup of US veterans. *Dig Dis Sci* 2008; 53:2719-22.
 52. Leung FW. Promoting informed choice of unsedated colonoscopy: patient-centered care for a subgroup of US Veterans. *Dig Dis Sci* 2008; 53:2955-9.
 53. Leung FW, Aharonian HS, Guth PH, Jackson G, Chu SK, Nguyen BD, et al. Unsedated colonoscopy: time to revisit this option? *J Fam Pract* 2008; 57:E1-E4.
 54. Leung FW. The case of unsedated screening colonoscopy in the United States. *Gastrointest Endosc* 2009; 69:1354-6.
 55. Redelmeier DA, Kahneman D. Patients' memories of painful medical treatments: real-time and retrospective evaluations of two minimally invasive procedures. *Pain* 1996; 66:3-8.
 56. Sanaka MR. Warm water irrigation is a useful technique during colonoscopy. *Am J Gastroenterol* 2008; 103:2655.
 57. Mizukami T, Hibi T. How I teach my trainees "water navigation colonoscopy". *Am J Clin Med* 2010; 7:144-6.
 58. Fennerty BM and Responses. Drown out that pain! Warm water infusions lead to better colonoscopy tolerance. *J Watch*. August 31st, 2010. Accessed 07052011.
 59. McCaulley MC. Colonoscopy keeps getting better. *Yampa Valley Medical Associates, P.C.* Accessed 07052011.
 60. Leung FW. Water exchange may be superior to water immersion for colonoscopy (invited editorial). *Clin Gastroenterol Hepatol* 2011; in press.