SYSTEMATIC REVIEW AND META-ANALYSIS

Water exchange colonoscopy increases adenoma detection rate: a systematic review with network meta-analysis of randomized controlled studies

Lorenzo Fuccio, MD,[1] Leonardo Frazzoni, MD,[1] Cesare Hassan, MD, PhD,[2] Marina La Marca, MD,[1] Valentina Paci, MD,[1] Veronica Smania, MD,[1] Nicola De Bortoli, MD,[3] Franco Bazzoli, MD,[1] Alessandro Repici, MD,[4] Douglas Rex, MD,[5] Sergio Cadoni, MD[6]

Bologna, Rome, Pisa, Rozzano, Iglesias, Italy; Indianapolis, Indiana, USA

Background and Aims: Water-aided colonoscopy techniques, such as water immersion (WI) and water exchange (WE), have shown different results regarding adenoma detection rate (ADR). We determined the impact of WI and WE on ADR and other procedural outcomes versus gas (air, AI; CO_2) insufflation colonoscopy.

Methods: A systematic search of multiple databases for randomized controlled trials comparing WI and/or WE with AI and/or CO_2 and reporting ADR was conducted. A network meta-analysis with mixed comparisons was performed. Primary outcome was ADR (overall, in the right side of the colon and by colonoscopy indication).

Results: Seventeen randomized controlled trials (10,350 patients) were included. WE showed a significantly higher overall ADR versus WI (odds ratio [OR], 1.31; 95% credible interval [CrI], 1.12-1.55) versus AI (OR, 1.40; CrI, 1.22-1.62) versus CO_2 (OR, 1.48; 95% CrI, 1.15-1.86). WE achieved the highest ADR also in the right side of the colon and in colorectal cancer screening cases (both significant vs AI and WI) as well as in patients taking a split-dose preparation (significant vs all the other techniques). The Boston Bowel Preparation Scale cleanliness score (vs AI and WI) was significantly higher for WE. Both WI and WE showed increased proportion of unsedated examinations and decreased real-time insertion pain, with WE being the least-painful insertion technique. Withdrawal time was comparable across techniques, but WE showed the longest insertion time (3-5 additional minutes).

Conclusions: WE significantly increases overall ADR, ADR in screening cases, and in the right side of the colon; it also improves colon cleanliness but requires a longer insertion time. (Gastrointest Endosc 2018;■:1-9.)

Water-aided colonoscopy (WAC) encompasses different techniques that entail infusion of water as an adjunct or in lieu of gas insufflation to distend the lumen during the insertion phase.[1] It is broadly categorized as water immersion or infusion (WI) and water exchange (WE).[1]

Numerous randomized controlled trials (RCTs) described WAC and refined what is meant by the terms WI and WE.[2-11] Accordingly, WE is a standardized technique developed to achieve gasless colonoscope insertion, substituting through infusion and near-simultaneous suction of water all colon content with a layer of clear water, allowing instrument progression to the cecum. This technique minimizes distension-related pain and maximizes colon cleanliness during insertion to increase the ease of withdrawal inspection.[1,12] Infused water is removed predominantly during insertion. On the other hand, WI is an unstandardized technique in which water is infused to facilitate cecal intubation.[2-6] WI does not entail suction removal of all dirty water, residual air, and feces during insertion and has been deemed too cumbersome and time-consuming.[2-4] Indeed, when judged to be safe, colonoscope insertion is done also in opaque water and/or air compartment.[2-4,13] Gas insufflation is used in limited amounts when necessary[2,5] or is resumed in the proximal colon to achieve cecal intubation.[13] Infused water is removed predominantly during withdrawal. With both techniques, withdrawal is usually carried out using gas insufflation.

Abbreviations: ADR, adenoma detection rate; AI, air; BBPS, Boston Bowel Preparation Scale; CI, confidence interval; CrI, credible interval; CRC, colorectal cancer; MD, mean difference; OR, odds ratio; RCT, randomized controlled trial; WAC, water-aided colonoscopy; WE, water exchange; WI, water immersion.

DISCLOSURE: *D. Rex, consultant for and the research support from Boston Scientific and Olympus. All authors disclosed no financial relationships relevant to this publication.*

0016-5107/$36.00
https://doi.org/10.1016/j.gie.2018.06.028

(footnotes continued on last page of article)

Adenoma detection rate (ADR) is an important colonoscopy quality indicator,[14] and its increase has been linked to a reduced risk of interval cancer[15] and death.[16] When analyzed separately, compared with gas insufflation colonoscopy (air [AI]) or CO_2, the impact of WI and WE on ADR differs.[1] WI achieved inconsistent results,[2-6,10] whereas WE has been shown to consistently increase ADR,[17-19] also in the right side of the colon.[10,20] However, these observations originated from studies with small sample sizes or with adenoma detection as a secondary outcome. Furthermore, either study design[21] or sample size[9,11] precluded demonstrating a significant difference between WE and WI.

Therefore, we conducted a systematic review and network meta-analysis to determine whether WI or WE is superior to AI and/or CO_2 in increasing ADR, also in the right side of the colon. We were also interested in the impact of these insertion techniques on colon cleanliness, which influences adenoma detection,[22-25] and other colonoscopy procedural outcomes.

METHODS

We followed the PRISMA guideline and checklist for reporting systematic reviews and network meta-analyses.[26] Data sources and search strategy, selection process, data extraction, and quality assessment are reported in detail in Appendix 1 (available online at www.giejournal.org).

Inclusion and exclusion criteria

A literature search was done to identify all relevant RCTs comparing WI and/or WE with AI and/or CO_2 insufflation published since 1999 as full text in English and including ADR among the outcomes. EMBASE, Medline, SCOPUS, and Cochrane Library were searched systematically for all articles that included the following terms in their titles, abstracts, or keyword lists: water-aided colonoscopy, water immersion colonoscopy, water exchange colonoscopy, air insufflation colonoscopy, carbon dioxide insufflation colonoscopy, and adenoma detection rate (see Appendix 1). References in retrieved articles were screened manually. Exclusion criteria included reviews, case reports, editorials, commentaries, articles involving only supervised trainees, articles including limited use of WI or WE in the distal colon, articles where WAC was performed with add-ons (devices, oil), and/or chromoendoscopy.

Outcomes assessment

The primary outcome was overall ADR[27] (defined as ADR from screening, surveillance, and diagnostic procedures) according to the colonoscopy technique and separately assessed in the entire and in the right side of the colon (cecum and ascending). Subgroup analyses in screening patients and by bowel preparation (ie, day-before or split-dose) were also carried out.

A key secondary outcome was bowel cleansing according to the Boston Bowel Preparation Scale (BBPS). Other secondary outcomes included cecal intubation time, withdrawal time (cases with and without polypectomies), proportion of complete unsedated procedures, real-time insertion pain, and adverse events. We used Cochrane's collaboration risk of bias tool to assess the risk of bias in all the included studies.[28]

Data analysis

First, we ran traditional meta-analyses with random effect models considering all studied outcomes for each colonoscopy technique separately to provide their absolute estimates. Data were summarized as pooled estimates of proportions for categorical outcomes and means for continuous outcomes, with 95% confidence interval (CI).

Second, we ran traditional pairwise meta-analyses with random effects models for all colonoscopy techniques compared within the included studies calculating the pooled estimates of odds ratio (OR) and 95% CI of direct comparisons between any 2 endoscopic techniques. Statistical heterogeneity was quantified with the I^2 statistic (high heterogeneity level >50%) and tested using the Cochrane Q^2 test (statistical significance level, $P < .1$). Publication bias was assessed by the Egger regression asymmetry test. For the Cochrane Q^2 test and the Egger test, a 2-sided $P < .05$ was regarded as significant.

Third, we conducted the network meta-analysis using the Bayesian Markov Chain Monte Carlo method. A random-effects model with noninformative priors comparable was used given the nature of network meta-analysis, encompassing tolerability to between-study heterogeneity and within-study variability. Direct and indirect evidence for all colonoscopy techniques were combined to estimate the studied outcomes, with a 95% equal tail credible interval (CrI).[29] Results were then presented as relative effects and Bayesian estimates of the probability that each technique has to be the best, the second best, the third best, and the worst relating to every studied outcome. All analyses were done with R software[30] by means of gemtc package[31] and metafor package.[32]

RESULTS

Our search identified 155 publications. Seventeen RCTs[2-6,9-11,17-21,33-36] were included in the analysis (41 arms of treatment, 10,350 patients; 55.7% male patients; Supplementary Figs. 1 and 2, available online at www.giejournal.org). Baseline characteristics of the included studies are reported in Table 1.

The raw proportions and means of the studied outcomes, stratified by each colonoscopy technique, are shown in Supplementary Table 2 (available online at www.giejournal.org) to provide their absolute magnitude. The results of multiple comparisons regarding all the