Title: Water Exchange Colonoscopy Decreased Adenoma Miss Rates in the Right and Proximal Colon: An Observational Study Using A Tandem Colonoscopy Approach

NCT Number: NCT03832322

Unique Protocol ID: EGH-2018

Date: Jan 3, 2019

STUDY PROTOCOL

BACKGROUND

Colonoscopy is currently regarded as the gold standard to detect and prevent colorectal cancer (CRC). It is widely practiced and generally safe and accurate, but not perfect. A substantial number of neoplastic lesions were missed according to back-to-back (tandem) air insufflation colonoscopy studies. In a systematic review of tandem colonoscopy studies, a 22% pooled miss-rate for adenomas were reported. Of all post-colonoscopy CRCs (PCCRCs), 58% were attributed to lesions missed during examination. Colonoscopy maneuvers helping to reduce AMR, particularly in the proximal and right colon, have the potential to decrease the incidence of PCCRCs.

Water exchange (WE) colonoscopy is characterized by the gasless insertion to the cecum in clear water and maximizing cleanliness during insertion. WE colonoscopy has been shown to improve the overall adenoma detection rate (ADR), compared to air insufflation colonoscopy. The impact of optimal WE with near-complete removal of infused water on proximal and right colon AMR has not been reported.

The primary outcomes of this study were the right and proximal colon AMRs determined by tandem colonoscopy using WE or CO2 insufflation for screening and surveillance indications. The secondary outcomes were the combined right and proximal colon AMR and hyperplastic polyp miss rate (HPMR), overall ADR and other adenoma detection related metrics between the two colonoscopy methods.

METHODS

This was an observational study comparing consecutive group of WE and CO2 insufflation in terms of right and proximal colon AMR by tandem colonoscopy. Consecutive patients were enrolled from July 2018 to November 2018 at Evergreen General Hospital, Taoyuan, Taiwan.

Participants

Consecutive patients aged 20 years or older undergoing colonoscopy for screening and surveillance indications were considered for enrollment. Exclusion criteria included familial adenomatous polyposis and hereditary non-polyposis CRC syndrome, personal history of inflammatory bowel disease, previous colonic resection, inability to achieve cecal intubation, obstructive lesions of the colon, poor colon preparation, inability to completely remove a polyp, gastrointestinal bleeding, allergy to fentanyl or midazolam, American Society of Anesthesiology classification of

physical status grade 3 or higher, mental retardation, pregnancy, and refusal to provide a written informed consent.

Bowel Preparation and Sedation

Patients were instructed to eat low-residual foods for two days before colonoscopy. All patients received a split dose of 3-L polyethylene glycol (Klean-Prep) for bowel preparation. Colonoscopy were performed with moderate sedation (intravenous fentanyl plus midazolam) administered by the colonoscopist.

First-pass Colonoscopy Procedure

Colonoscopies are performed by two board-certified colonoscopists (Chi-Liang Cheng, Yen-Lin Kuo) using a standard colonoscopy (CF-Q260AL/I; Olympus Medical Systems Corp., Tokyo, Japan). Felix W. Leung was involved in the study design, data analyses, and report preparation, but not in patient enrollment. Colonoscopy began with the patients in the left lateral position. In the WE group, the air pump was turned off before starting the procedure. During the insertion phase, air and residual water or feces in the rectum were aspirated, and then the colon was irrigated with water using flushing pumps (Olympus AFU-100; Olympus Corp.). There was no restriction placed on the overall volume of water infused to achieve adequate cleansing. WE entailed the infusion of water to open the lumen and sequential suction of water. Air pockets, when encountered, was aspirated. When the cecum was reached and after most of the water was suctioned to collapse the cecal lumen, CO2 was opened. In the CO2 group, colonoscopy was performed in the usual fashion, with minimal insufflation required to aid insertion. Cleaning in the CO2 group was predominantly performed during withdrawal. Polyp resection was done during insertion and withdrawal in both groups.

Second-pass Colonoscopy Procedure

After the first complete withdrawal of the colonoscope, a second colonoscopic examination aided by CO2 insufflation during insertion and withdrawal was performed by the same endoscopist. In both groups, the colonoscope was reinserted into the cecum as quickly as possible, and the entire colon was re-examined. Polyp resection was carried out during insertion and withdrawal in both groups during the second-pass examination. All polyps identified in the second-pass examination were defined as missed polyps with the exception of the diminutive polyps in the rectosigmoid colon that remain after the first-pass colonoscopy.

Definition

Complete colonoscopy was defined as successful cecal intubation. Insertion time was defined as the time between the scope insertion and cecal intubation. Withdrawal time was defined as the time from cecal intubation to the time when the colonoscope was withdrawn from the anus, including the time taken for mucosal cleaning and polypectomy. Total procedure time was the sum of insertion time and withdrawal time. A Poor colon preparation was defined as a total BBPS score of 5 or less.

All colonic polyps removed during procedures were sent for histological examination with clear labeling of location and sequences of colonoscopy. The location of colonic polyps was defined according to the anatomical distribution. Right colon was defined as cecum, ascending colon, and hepatic flexure. Proximal colon was defined as right and transverse colon. Diminutive polyps were defined as polyps with size ≤5 mm. Small polyps were defined as polyps with size 6-9 mm. Large polyps were defined as polyps with size ≥10 mm. Adenomas included all adenomas and sessile serrated adenoma. Advanced adenomas were defined as those lesions with one of the following criteria: 1) lesions larger than 10 mm in diameter; 2) lesions with a villous component; 3) lesions with high-grade dysplasia; and 4) lesions with invasive features.

Lesions detected on the first-pass examination were used for the calculation of adenoma detection. ADR was defined as the proportion of colonoscopies where at least one adenoma was found. Proximal hyperplastic polyp detection rate (PHP-DR) was defined as the proportion of patients undergoing colonoscopy in whom at least one hyperplastic polyp was identified in the proximal colon.

Lesions detected on the second-pass examination were used for the calculation of adenoma or polyp miss. AMR and HPMR were calculated as the number of adenomas and hyperplastic polyps missed in the first colonoscopy divided by the total number of adenoma and hyperplastic polyps detected during both the first and second colonoscopies.

STATISTICAL ANALYSIS PLAN

Sample size estimation

The sample size estimation was based on the assumption that WE colonoscopy reduced proximal colon AMR compared to conventional CO2 insufflation colonoscopy. We estimated the proximal colon AMR in the CO2 group to be 30% and the average detected number of proximal colon adenoma to be 0.9 per subject after first colon examination. To show a clinically important improvement of proximal colon AMR reduction by the WE colonoscopy, we assumed that WE colonoscopy should reduce the AMR by 18%. With a statistical power of 80% and a two-side significance level of 0.05, 82 patients were needed in each study arm.

Statistical analysis

Summary statistics were presented as frequencies and percentages in the case of categorical variables and as the means with standard deviations (SD) in the case of continuous variables. Student's *t*-test for continuous factors, Wilcoxon rank sum test for ordinal variables (such as polyp size), and Chi-square test for categorical variables were used to assess differences in demographic and clinical characteristics of patients in each group. All statistical analyses were performed by using SAS version 9.3 or later (SAS Institute Inc., Cary, NC, USA). The criterion for statistical significance will be *P* value <0.05.