

Study Title: I-SCAN FOR ADENOMA DETECTION

Study has been registered on ClinicalTrials.gov: NCT02811419

Date: January 5, 2017

STUDY PROTOCOL

METHODS

Study design and setting

We will perform a prospective, randomized controlled trial comparing i-scan 1 (surface enhancement with contrast enhancement) with conventional HDWL during colonoscopy for the detection of colorectal neoplasia; a representative example of endoscopic images using i-scan 1 and HDWL is shown in Figure 1. The study will be conducted at the University of California, San Francisco (UCSF), an academic, tertiary care medical center serving over 1.2 million patients annually in the San Francisco Bay Area.

Study eligibility

Patients will be recruited between February 1, 2017 and December 31, 2017. Inclusion criteria included patients ages 50 to 75 years who were scheduled for outpatient colonoscopy for the indications of CRC screening, post-polypectomy surveillance, or diagnostic workup for a positive fecal-based test (FIT). Exclusion criteria were inpatients and patients with inflammatory bowel disease, colorectal cancer, polyposis syndromes, previous surgical resection of any portion of the colon or rectum, and patients referred for endoscopic mucosal resection of previously diagnosed colorectal polyps.

Randomization

Patients will be randomized (1:1) to HDWL alone or i-scan 1 during colonoscopy. The randomization order will be determined by using a computer-generated sequence in block sizes of 30. Sealed, opaque envelopes containing the randomization assignment will be prepared by one investigator. After obtaining informed consent from the patient, the envelope will be opened to reveal the randomization assignment prior to beginning the procedure.

Colonoscopy procedure

All patients will need to complete a bowel preparation using split-dose US Food and Drug Administration-approved preparations. Four attending physicians, each of whom performed over 500 colonoscopies the year prior, will perform withdrawal in every procedure. Insertion of the colonoscope and withdrawal from cecum will be performed with the assigned imaging modality (i.e., HDWL or i-scan 1). The i-scan 1 setting that will be used will be the “out of the box” setting (supplementary table) that is standard with Pentax colonoscopes (Pentax EC-3890 and EC-3490); no adjustments will be made to the setting. If a lesion/polyp were detected, the physician will be permitted to change from i-scan 1 to HDWL and vice versa at their discretion to interrogate and better characterize the lesion/polyp per their routine practice. Once the lesion/polyp is removed and retrieved, the physician can return to the assigned imaging modality for inspection. Withdrawal time will be measured from the time withdrawal from the cecum began to the end of the examination – the time will not be “paused” for polyp resection. Withdrawal time during a negative colonoscopy exam (one in which no polyps were identified and no interventions were performed), called the “negative withdrawal time,” will also be separately analyzed. Resected polyps will be sent for pathologic examination as part of routine clinical care.

Outcome measurement

The primary outcome measured will be the ADR, defined as the proportion of subjects with at least one traditional adenoma (including tubular or villous adenomas, and adenomas with high grade dysplasia or adenocarcinoma) of any size. Secondary outcomes measured included the adenomas per colonoscopy (APC), serrated adenoma detection rate (SDR), defined as the proportion of subjects with at least one serrated polyp (serrated adenoma or traditional serrated

adenoma) of any size as well as the neoplasia detection rate (NDR), defined as the percentage of colonoscopies in which at least one traditional adenoma or serrated adenoma was found.

Additionally, the location, size, morphology and number of polyps will also be recorded. Flat polyps will be defined as flat appearing polyps, in which the height was less than two times the diameter. Histology of polyps will be evaluated by expert gastrointestinal pathologists at UCSF, who will be blinded to the specific endoscopic diagnosis and the histopathological diagnosis was used as the gold-standard. High risk adenomas will be defined as an adenoma of any size with high grade dysplasia or a villous component, an adenoma greater than ten millimeters in size, adenocarcinoma, and, or three or more adenomas of any size found on a single colonoscopy.

Sample size and statistical analysis

The sample size calculation for the primary outcome of ADR was based on the average ADR of our group over the previous two years of 30%, which we estimated would be the control (HDWL) group's ADR. We estimated a 10% difference between groups based on a previous study²³. To achieve an absolute difference of 10% in the ADR between groups with a statistical type I error of 5% (two-sided) and power of 80%, a minimum of 356 patients per group was needed (712 patients total). Adjusting for a 4% drop-out due to bowel prep or inability to intubate the cecum, we targeted enrollment of 740 patients.

Intention-to-treat analysis will be used to assess the primary and secondary outcomes. We will also perform per-protocol analyses to explore differences in the primary and secondary outcomes after excluding patients with preparations that were considered too difficult to correct with intra-procedural washing (i.e., Boston bowel prep score < 2 in any segment). Only patients with a complete procedure and adequate bowel preparation will be included in the per-protocol analyses. Categorical data will be compared by the χ^2 -test or Fisher Exact test where appropriate

and numerical data will be compared by the Student's t-test. Statistical significance will be defined as a two-sided p-value < 0.05 .

Study oversight

The study was approved by the UCSF institutional review board. All patients provided informed consent. The study was registered on ClinicalTrials.gov (NCT02811419).