SYSTEMATIC REVIEWS AND META-ANALYSES

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Accuracy of First- and Second-Generation Colon Capsules in Endoscopic Detection of Colorectal Polyps: A Systematic Review and Meta-analysis

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BACKGROUND & AIMS: **Colon capsule endoscopy (CCE) is a noninvasive technique used to explore the colon without sedation or air insufflation. A second-generation capsule was recently developed to improve accuracy of detection, and clinical use has expanded globally. We performed a systematic review and meta-analysis to assess the accuracy of CCE in detecting colorectal polyps.**

METHODS: **We searched MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, and other databases from 1966 through 2015 for studies that compared accuracy of colonoscopy with histologic evaluation with CCE. The risk of bias within each study was ascertained according to Quality Assessment of Diagnostic Accuracy in Systematic Reviews recommendations. Per-patient accuracy values were calculated for polyps, overall and for first-generation (CCE-1) and second-generation (CCE-2) capsules. We analyzed data by using forest plots, the I^2 statistic to calculate heterogeneity, and meta-regression analyses.**

RESULTS: **Fourteen studies provided data from 2420 patients (1128 for CCE-1 and 1292 for CCE-2). CCE-2 and CCE-1 detected polyps >6 mm with 86% sensitivity (95% confidence interval [CI], 82%–89%) and 58% sensitivity (95% CI, 44%–70%), respectively, and 88.1% specificity (95% CI, 74.2%–95.0%) and 85.7% specificity (95% CI, 80.2%–90.0%), respectively. CCE-2 and CCE-1 detected polyps >10 mm with 87% sensitivity (95% CI, 81%–91%) and 54% sensitivity (95% CI, 29%–77%), respectively, and 95.3% specificity (95% CI, 91.5%–97.5%) and 97.4% specificity (95% CI, 96.0%–98.3%), respectively. CCE-2 identified all 11 invasive cancers detected by colonoscopy.**

CONCLUSIONS: **The sensitivity in detection of polyps >6 mm and >10 mm increased substantially between development of first-generation and second-generation colon capsules. High specificity values for detection of polyps by CCE-2 seem to be achievable with a 10-mm cutoff and in a screening setting.**

Keywords: Imaging; PillCam; Colorectal Cancer Screening; Colorectal Cancer.

Abbreviations used in this paper: **AUC, area under the curve; CCE, colon capsule endoscopy; CI, confidence interval; CRC, colorectal cancer; DOR, diagnostic odds ratio; FDA, Food and Drug Administration; FOBT, fecal occult blood test; LR, likelihood ratio; MeSH, medical subject headings; NLR, negative likelihood ratio; PEG, polyethylene glycol; PLR, positive likelihood ratio; PMDA, Pharmaceuticals and Medical Device Agency; QUADAS, Quality Assessment of Diagnostic Accuracy in Systematic Reviews; SROC, summary receiver operating characteristic curve.**

Most current article

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Colon capsule endoscopy (CCE), introduced in 2006, has generated great expectations,[1] but the enthusiasm for this new, noninvasive technique able to explore the colon without sedation and air insufflation was mitigated when the first studies were published.[2,3] Compared with colonoscopy, the first generation of CCE was shown to be a feasible and safe imaging test of the colon. However, sensitivity for clinically meaningful lesions, ie, ≥6 mm polyps or masses, appeared to be suboptimal.[2–4] For this reason, a second-generation capsule (CCE-2) was developed.[5,6] New technology was implemented; in particular, the capsule frame rate increased from 4 to 35 images per second to adequately image the mucosa when the capsule is accelerated by peristalsis. The angle of view also increased from 156° to 172° for each lens to cover nearly 360° of the colon surface. The Data Recorder (DR3) was also improved by simplifying the procedure.

For both generation capsules, ambitious claims mostly are based on relatively few within-subject comparisons with colonoscopy from single centers.[7] These studies vary considerably in terms of study design, selected population, and technical performances of the colon capsule. Moreover, although the second generation is believed to have higher accuracy when compared with the first generation of colon capsule, this assumption was never systematically demonstrated.

A core body of evidence now exists for CCE-2, including pivotal trials in the United States and Japan that were recently published.[8,9] These trials prompted the U.S. Food and Drug Administration (FDA) and the Japanese Pharmaceuticals and Medical Device Agency (PMDA) to recently clear the device for use in these countries. Furthermore, in 2016 the FDA further expanded the indication for the second-generation capsule. Performing a meta-analysis is necessary to more thoroughly understand the performance of CCE-2 across varied studies and assess its differences from the older and underperforming CCE-1, where misconceptions may still reside around the accuracy of the first versus second generation.

The aim of this systematic review and meta-analysis was to assess CCE accuracy as verified with within-subjects colonoscopy in detecting colorectal lesions and to compare the performance of the first and second generations of colon capsule.

Methods

Methods of analysis and inclusion criteria were based on PRISMA recommendations.[10]

Eligibility Criteria

We considered all clinical studies (involving human subjects) from 1966 to September 15, 2015, in which accuracy of CCE for colorectal polyps was assessed by using colonoscopy with histology as comparator. Animal and review studies were excluded. If there was any suspicion of cohort overlap between studies, only the most recent study was included.

Information Sources

Relevant original publications (in English language) were identified in MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials and in the abstract publications of the largest medical conferences on this topic (Digestive Disease Week and United European Gastrointestinal Week). Prespecified Medical Subject Headings (MeSH) and non-MeSH terms were used for the search and are reported in Supplementary Material. Both full texts and abstracts were included. Abstracts were included to minimize publication bias. Additional publications were identified through searching the reference lists of retrieved articles. A full list of retrieved studies and the reason for exclusion are in Supplementary Table 1. When further information from selected articles was needed to clarify methodology/data of included studies, we attempted to contact the authors (Supplementary Table 2).

Study Selection

All titles and abstracts of articles retrieved in the prespecified search were independently screened by 2 reviewers (C.H., C.S.). By using the full report of the study, studies were evaluated for inclusion in the analysis. The following inclusion criteria were applied: (1) use of colon capsule, (2) detection of polyps/neoplasia as study end point, (3) colonoscopy with histology used as reference standard, and (4) possibility to extract data from 2 × 2 tables to define CCE accuracy. Exclusion criteria were (1) inflammatory bowel disease–related CCE study with end points other than sporadic neoplasia, (2) suboptimal reference standard such as computed tomography colonography or fecal tests, and (3) poor quality of data preventing an adequate extraction. Any disagreements were resolved through consensus. Data were extracted from the included studies by 1 reviewer (C.S.) and checked by 1 of the second reviewers (C.H., J.A.L., R.P., S.A.G., F.S.S.), and the data were extracted into tables. Any disagreements were resolved through discussion with a third reviewer (S.P.).

Data Collection Process and List of Items

From each article, the reviewers independently abstracted the following information: (1) year of publication; 2) type of publication (full text/abstract); 3) country(ies); (4) number of centers; (5) study design (prospective/retrospective/mono-/multi-center); (6) generation of CCE (1 vs 2); (7) polyethylene glycol (PEG) volume administered; (8) type and volume of booster; (9) matching rule between CCE and colonoscopy adopted (if any); (10) availability of either or both per-patient and per-polyp analysis; (11) timing of colonoscopy (same day