Accuracy of Capsule Colonoscopy and Computed Tomographic Colonography in Individuals With Positive Results From the Fecal Occult Blood Test

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BACKGROUND & AIMS: **Computed tomographic colonography (CTC) is a reliable option for screening subjects who are unable or unwilling to undergo optical colonoscopy (OC). A colon capsule (PillCam Colon2 [CC2]; GivenImaging Ltd., Yokneam, Israel) has shown promising results in detecting polyps larger than 6 mm. We compared the accuracy of CC2 and CTC in identifying individuals with at least 1 polyp greater than 6 mm and subjects' attitude toward the procedures.**

METHODS: **Fifty individuals (mean age, 59.2 ± 5.8 y; 58% male) with positive results from the immunochemical fecal occult blood test (iFOBT-positive) underwent CC2, CTC, and OC. The unblinded colonoscopy, integrating OC, CTC, and CC2 results, was used as the reference standard. In a per-patient analysis, the accuracy of CC2 and CTC were assessed for individuals with at least 1 polyp 6 mm or larger. Individuals were asked to choose which procedure they would be willing to repeat between CTC and CC2.**

RESULTS: **The combination of OC, CTC, and CC2 identified 16 cases with at least 1 polyp 6 mm or larger (reference standard). CTC identified the polyps with 88.2% sensitivity, 84.8% specificity, a 3.0 positive likelihood ratio, and a 0.07 negative likelihood ratio. CC2 identified the polyps with 88.2% sensitivity, 87.8% specificity, a 3.75 positive likelihood ratio, and a 0.06 negative likelihood ratio. Thirty-nine subjects (78%) said they preferred CC2 to CTC.**

CONCLUSIONS: **CC2 and CTC detect polyps 6 mm and larger with high levels of accuracy; these techniques are effective in selecting iFOBT-positive individuals who do not need to be referred for colonoscopy. CC2 seems to be better tolerated than CTC, and could be a reliable alternative to CTC for iFOBT-positive individuals who are unable or unwilling to undergo OC. ClinicalTrials.gov number: NCT01744509.**

Keywords: Capsule Colonoscopy; Computer Tomographic Colonography; Optical Colonoscopy; Colon Cancer; Early Detection.

Colorectal cancer (CRC) is a major cause of morbidity and mortality in Western countries, although several studies have shown that optical colonoscopy (OC) is the key tool in reducing CRC mortality.[1] Unfortunately, OC is still perceived as a painful, invasive, and unpleasant procedure. Indeed, when it is offered as the primary screening method, the cumulative participation rate is low (range, 3%–17%).[2,3]

In patients unable or unwilling to undergo OC, computed tomographic colonography (CTC) is offered as a first-line examination. In patients with increased risk for CRC, it has been shown that CTC has a diagnostic accuracy comparable with OC.[4] Furthermore, several meta-analyses[5] have shown that the sensitivity of CTC for polyps 10 mm or larger exceeds 85%, although sensitivity decreases for small and diminutive polyps. In addition, CTC was reported to have a higher patient acceptability when compared with OC.[6]

Recently, a colon capsule has been marketed and quickly implemented, with the second-generation colon capsule (PillCam Colon2 [CC2]) showing higher sensitivity in detecting polyps larger than 6 and 10 mm (89%

Abbreviations used in this paper: CC2, PillCam Colon2; CI, confidence interval; CRC, colorectal cancer; CTC, computed tomographic colonography; FN, false negative; FP, false positive; iFOBT-positive, positive results from the immunochemical fecal occult blood test; LR, likelihood ratio; OC, optical colonoscopy; RS, reference standard.

1542-3565/$36.00
http://dx.doi.org/10.1016/j.cgh.2013.12.027

and 88%, respectively).[7,8] Furthermore, in those patients declining OC as a screening test, the availability of capsule colonoscopy could increase CRC screening adherence.[9]

This pilot study was designed to assess CTC and CC2 accuracy in identifying positive results from the immunochemical fecal occult blood test (iFOBT-positive) in individuals with at least 1 polyp 6 mm or greater, comparing both these procedures with a new reference standard (RS) that integrated CTC, OC, and CC2 results.

Materials and Methods

Subjects participating in the national CRC screening program (age, 50–69 y), with a positive iFOBT result, were offered the option to undergo OC during an interview with a gastroenterologist. Those who accepted and did not present any exclusion criteria were eligible for the study (Table 1). If the subject agreed to participate, the 3 diagnostic procedures (CC2, CTC, and OC) were scheduled according to the study design; if the patient declined, according to the screening program, the OC alone was planned.

The study was supported by the Fondazione Cariplo (http://www.fondazionecariplo.it/en). The authors designed the study and gathered and analyzed data; the sponsor did not participate in the design or conduction of the study, and did not review or approve the data. All the authors reviewed and approved the final manuscript.

The study met the Declaration of Helsinki criteria; it was approved by the local Ethics Committee and was registered at www.clinicaltrial.gov (NCT01744509).

Study Design and Reference Standard

Participating individuals underwent CC2, CTC, and OC. The procedures were scheduled as follows: first, the patient underwent the CC2, and, about 15 days later, the patient underwent CTC early in the morning, followed by OC later that day.

At the time of OC, the endoscopist was blind to the CC2 and CTC results. After inspecting the right colon the endoscopist was informed about the CTC and CC2 findings in that segment. If 1 of the 2 tests (CTC or CC2) discovered any finding that was not reported by the OC operator, the endoscopist was asked to re-inspected the right colon. This procedure was repeated for the 3 colonic segments. This procedure, which integrated results of the OC, CTC, and CC2, defined as a double unblinded colonoscopy, was our RS.

Polyps identified by the RS were sized during the OC (measurements were taken in vivo by comparison with a 5-mm open forceps or with an open snare).

Table 1. Inclusion and Exclusion Criteria

Inclusion criteria
Subjects participating in the national CRC screening program (age, 50–69 y) with positive iFOBT
Exclusion criteria
Dysphagia or swallowing disorders
Congestive heart failure
Known renal insufficiency
Prior major abdominal surgery of the gastrointestinal tract
Known or suspected small-bowel obstruction
Presence of a cardiac pacemaker or other implanted electromedical devices
Allergy/contraindication to medications used in the study

Outcomes and Matching Rules

The primary end point of the study was to evaluate CC2 and CTC accuracy for the identification of individuals with at least 1 polyp 6 mm or larger. When CTC or CC2 showed at least 1 polyp 6 mm or larger, which was confirmed by the RS, the individual was classified as true positive. If neither the comparative test nor the RS identified at least 1 polyp 6 mm or larger, the individual was classified as true negative. The individual was categorized as false positive (FP) when the CTC or CC2 identified at least 1 polyp 6 mm or larger, not confirmed by the RS, and, conversely, as false negative (FN) if the polyp was missed by the CC2 or CTC. When 2 or more polyps were detected in the same individual, the largest one was considered. The calculation was repeated by setting the polyp threshold to 10 mm or larger.

When a polyp was identified by the RS and by CTC or CC2 but there was a difference in size, according to the size threshold, the individual was classified by definition as FP (if the polyp identified by the RS was smaller) or FN (if the polyp identified by the RS was larger). In case of size discrepancy, we directly compared polyp pictures with those taken during OC. When, despite differences in size (taking into account shape and texture surface) the polyp was obviously the same, it was defined as a size mismatch.

Individual Preference

All the individuals fulfilled a self-administered questionnaire that asked 2 questions: “Between CTC and CC2, which examination are you willing to repeat in the future?” and “Please clarify the reason.”

Capsule Colonoscopy

Capsule colonoscopy was performed by means of CC2. The preparation regimen is detailed in Table 2. The individuals were instructed to remove the sensor array either at time of capsule excretion, or 12 hours after capsule ingestion, whichever occurred first.

Colon cleansing was graded for the left, transverse, and right colon by means of a 4-point scale (excellent, good, fair, or poor).[10] When 1 or more segments were graded as poor/fair, the preparation was graded as inadequate.