

Endotics system vs colonoscopy for the detection of polyps

Emanuele Tumino, Rodolfo Sacco, Marco Bertini, Michele Bertoni, Giuseppe Parisi, Alfonso Capria

Emanuele Tumino, Rodolfo Sacco, Marco Bertini, Michele Bertoni, Giuseppe Parisi, Alfonso Capria, Operative Unit of Gastroenterology and Metabolic Diseases, Department of Gastroenterology, Pisa University Hospital, Via Paradisa 2, 56124 Pisa, Italy

Rodolfo Sacco, Institute of Internal Medicine, University of Foggia, Viale Pinto, 71100 Foggia, Italy

Author contributions: Tumino E research design, endoscopist, data collection and analysis, work drafting; Sacco R research design, data collection and analysis, work drafting; Bertini M data collection and statistical analysis, endoscopist; Bertoni M, Parisi G data collection and clinical care, endoscopists; Capria A research design, work drafting.

Correspondence to: Dr. Emanuele Tumino, Operative Unit of Gastroenterology and Metabolic Diseases, Department of Gastroenterology, Pisa University Hospital, Via Paradisa 2, 56124 Pisa, Italy. e.tumino@ao-pisa.toscana.it

Telephone: +39-50-997419 Fax: +39-50-997412

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Abstract

AIM: To compare the endotics system (ES), a set of new medical equipment for diagnostic colonoscopy, with video-colonoscopy in the detection of polyps.

METHODS: Patients with clinical or familial risk of colonic polyps/carcinomas were eligible for this study. After a standard colonic cleaning, detection of polyps by the ES and by video-colonoscopy was performed in each patient on the same day. In each single patient, the assessment of the presence of polyps was performed by two independent endoscopists, who were randomly assigned to evaluate, in a blind fashion, the presence of polyps either by ES or by standard colonoscopy. The frequency of successful procedures (i.e. reaching to the cecum), the time for endoscopy, and the need for sedation were recorded. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the ES were also calculated.

RESULTS: A total of 71 patients (40 men, mean age

51.9 ± 12.0 years) were enrolled. The cecum was reached in 81.6% of ES examinations and in 94.3% of colonoscopies ($P = 0.03$). The average time of endoscopy was 45.1 ± 18.5 and 23.7 ± 7.2 min for the ES and traditional colonoscopy, respectively ($P < 0.0001$). No patient required sedation during ES examination, compared with 19.7% of patients undergoing colonoscopy ($P < 0.0001$). The sensitivity and specificity of ES for detecting polyps were 93.3% (95% CI: 68-98) and 100% (95% CI: 76.8-100), respectively. PPV was 100% (95% CI: 76.8-100) and NPV was 97.7% (95% CI: 88-99.9).

CONCLUSION: The ES allows the visualization of the entire colonic mucosa in most patients, with good sensitivity/specificity for the detection of lesions and without requiring sedation.

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Key words: Colonoscopy; Diagnosis; Endotics system; Polyps; Sedation

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INTRODUCTION

Video-colonoscopy is considered the gold-standard for the diagnosis of colonic diseases, including carcinomas and polyps^[1]. However, this diagnostic technique presents some limitations, such as invasiveness and patient discomfort, which limit the adherence to programs for the early detection of colon carcinoma^[2,3]. When undergoing colonoscopy, patients often require sedation, which may result

in the onset of unintended deep sedation^[4]. In addition, standard colonoscopy is associated with various procedural risks, ranging from minor complications^[5] to cardiopulmonary events^[6,7], colon perforation^[8,9], infections^[10,11] and, in very rare circumstances, death^[12].

Newer diagnostic techniques are therefore advocated to overcome these limitations while maintaining a good diagnostic accuracy^[1,13]. While the use of such techniques in clinical practice is starting to emerge, direct head-to-head comparisons between different technologies are still lacking^[1].

The endotics system (ES) is a new robotic device composed of a workstation and a disposable probe, which gave promising results in a pilot study for the detection of colonic polyps^[14]. We report here the results of a head-to-head comparison of ES and standard colonoscopy in the diagnosis of polyps. To our knowledge, this is the first direct comparison of these techniques.

MATERIALS AND METHODS

Study setting and design

This is a prospective, single-centre study conducted at the Department of Gastroenterology of Pisa University Hospital, from March to August 2009. All patients gave informed consent before inclusion in the trial. The study was conducted in accordance to the Helsinki Declaration (2008 version) and its protocol was approved by the Hospital Ethical Committee.

Eligibility criteria

All adult patients (aged 18-75 years) consecutively seen at our Unit were eligible for this study if they met ≥ 1 of the following criteria: (1) age > 40 years with at least a first-grade relative with a previous diagnosis of colorectal carcinoma or adenoma before he/she was 60 years old; (2) were receiving follow-up evaluations after previous endoscopic polypectomy; and (3) were positive at faecal occult blood test (FOBT), as assessed during screening campaigns. Patients were excluded if they were pregnant, affected by chronic renal insufficiency, active ulcerative colitis or Crohn's disease, bleeding lesions of oesophagus, stomach or small intestine, or had undergone abdominal surgical interventions in the 6 mo period prior to study entry.

The ES

The ES (Era Endoscopy S.r.l., Pisa, Italy) is a new CE-marked (the CE marking certifies that a product has met EU consumer safety, health or environmental requirements) medical device for diagnostic colonoscopy, composed of a workstation and a hand-held console which drives a steerable probe through the colon lumen. A complete description of this device has been provided elsewhere^[14]. In this study we used a slightly different ES version from the one used in the previous pilot study (25 cm length in the contracted form and 43 cm in the elongated form, with respect to 23 and 37 cm, respectively, of the previous version).

ES probe is sterile, disposable and soft, in order to allow for adjustment of its shape to colon morphology, and avoid stretching maneuvers to reach the cecum. The probe is composed of a head, a steerable tip, a flexible body (all with 17 mm diameter), a thin tail (7.5 mm diameter and 180 cm length) and a special tank with an electro-pneumatic connector. The head hosts both a vision system, including a camera (110° vision angle) with LED light sources, and channels for water jet and air in order to provide rinsing and suction/insufflation, respectively. The workstation allows the endoscopist to drive the probe using the console and to visualize real-time images on a screen.

The key operations performed by the ES can be summarized as follows: (1) the steering, consisting of an electro-pneumatically driven deflection of the head of the robot (a rotation of 180° can be performed in every direction within a short bending diameter); (2) the elongation of the probe body, visually driven by the endoscopist in order to follow the morphology of the intestine; and (3) the control of rinsing, insufflation and suction. Suction allows the endoscopist to remove liquids from the bowel and convey them to the tank. Insufflation may help unfold the bowel wall in order to have a clearer view of the mucosa.

The motion of advancing the probe through the colon follows a cyclic sequence of steps^[14].

Study procedures

All patients underwent a standard preparation to colonoscopy: a fiber-free diet in the seven days preceding the examination and oral administration of phosphate sodium lavage solution (80 mL in 2000 mL of water until evacuation of clear yellowish fluid) on the day before the examination. Both ES examination and standard colonoscopy were performed in each patient on the same day. All procedures were performed by endoscopists with a solid experience (> 500 colonoscopies successfully performed) and after complete training with the ES (> 20 tests on pigs or models). In all patients, the first colonic examination was performed with the ES; after that, the patients underwent standard colonoscopy. This sequence was decided in order to avoid possible alterations of the physiologic features of the colon due to standard colonoscopy. Moreover, the current version of the ES does not allow us to perform polypectomy or biopsies; these procedures, if required, have been performed during the standard colonoscopy. Each patient was examined lying on his/her left side and were later turned to the supine position only if required.

In each single patient, the assessment of the presence of polyps was performed by two independent endoscopists, who were randomly assigned to evaluate, in a blind fashion, the presence of polyps either by ES or by standard colonoscopy. The randomization was performed according to a list of numbers generated by a computer and each operator ignored the results of the evaluation performed by the other examiner.

The colonoscopy was judged successful upon the visual recognition of the ileo-cecal valve by the examiner, confirmed by a third independent endoscopist. The di-

Table 1 Demographic characteristics and indications for colonoscopy

Parameter	Value
Total No. of patients (<i>n</i>)	71
Males, <i>n</i> (%)	40 (56.3)
Age (yr), mean ± SD, (range)	51.9 ± 12.0 (33-81)
Indication for colonoscopy, <i>n</i> (%)	
Follow-up of a previous polypectomy	11 (15.5)
Search for faecal occult blood	21 (29.5)
Familiar history of colon neoplasms	39 (54.9)

Table 2 Operative results observed with the endotics system procedure and with standard colonoscopy (*n* = 71 for each procedure) *n* (%)

Parameter	Endotics system	Standard colonoscopy	<i>P</i> value
Procedures reaching cecum	58.0 (81.6)	67.0 (94.3)	0.0300
Complete procedure, mean ± SD (min)	45.1 ± 18.5	23.7 ± 7.2	< 0.0001
Patients requiring sedation	0	14.0 (19.7)	< 0.0001

mensions and sites of the polyps identified during the ES and the standard colonoscopy were recorded. Polyps were then removed and/or biopsies were taken as necessary, according to polyp shape and dimensions. Polyp dimensions were estimated as described by Van Gossum *et al*¹⁵. Colon cleansing was assessed according to Aronchick's scale and recorded¹⁶. The time required to perform ES and colonoscopy were also measured. All the patients were contacted 1 and 7 d after the procedures to evaluate the possible onset of adverse events.

Antispasmodic medications were not allowed. Midazolam and meperidine were administered and tailored according to each patient's need. These medications were offered to patients who referred pain during either ES or standard colonoscopy.

Data analysis

All the data were analyzed by descriptive statistics, as appropriate. Comparisons between ES and standard colonoscopy results were performed by Student's paired *t*-test or Fisher's exact test, with a *P* value < 0.05 considered statistically significant. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the ES were calculated with standard 2 × 2 table analysis.

All statistical analyses were performed with SAS software (SAS Institute, Cary, NC).

RESULTS

A total of 71 patients (40 men; mean age 51.9 ± 12.0 years, Table 1) were included in the study and underwent both ES procedure and standard colonoscopy.

Operative results of the two procedures are summarized in Table 2. Overall, the cecum was reached more frequently with standard colonoscopy (*P* = 0.03 vs ES);

Table 3 Reasons for incomplete views of the colon during examinations *n* (%)

Reasons	Endotics system	Standard colonoscopy
Anal stenosis	1 (1.4)	0
Sigma stenosis	2 (2.8)	0
Dolicolon	0	1 (1.4)
System failure	3 (4.2)	0
Insufficient length of endoscopic device	1 (1.4)	0
Insufficient cleaning	6 (8.4)	3 (4.2)

moreover standard colonoscopy required a significantly shorter time with respect to ES (*P* < 0.0001). On the other hand, no patients requested sedation during the ES procedure, while 14 subjects (19.7%) requested the administration of midazolam and meperidine during standard colonoscopy (*P* < 0.0001).

Diagnostic accuracy

In total, 14 patients were excluded from the analysis of diagnostic accuracy, as a complete view of the colon was not obtained in them with ES and/or standard colonoscopy (Table 3).

Overall, 14 polyps were detected during ES procedure and 15 were identified during standard colonoscopy. The measured mean diameter of the polyps was comparable with the two procedures (7.64 ± 3.82 mm for ES, 7.50 ± 3.18 mm for standard colonoscopy).

Sensitivity of ES, with respect to standard colonoscopy, was 93.3% [95% confidence interval (95% CI): 68.0-99.0], and specificity was 100% (95% CI: 76.8-100). PPV and NPV were 100% (95% CI: 76.8-100) and 97.7% (95% CI: 88.0-99.9), respectively.

Adverse events

Six patients (8.4%) reported adverse events (nausea, headache, abdominal pain and discomfort). All events were of mild intensity and a spontaneous recovery occurred within 48 h from the onset in all cases. As the onset of adverse events was evaluated 1 and 7 d after the colonoscopy procedures and one single cleaning solution was used, it was not possible to distinguish between adverse events occurring during ES examination and those occurring during standard colonoscopy.

DISCUSSION

Overall, the results of this study suggest that the ES procedure may represent an accurate tool for the detection of colon polyps. Despite the fact that ES was not able to reach the cecum in some cases and was longer than the standard colonoscopy, it had a comparable diagnostic accuracy and did not require the administration of sedating drugs.

It is widely accepted that standard colonoscopy is associated with the possible onset of adverse events and with a low acceptance by patients²⁻¹². Newer technologies for colonoscopy are therefore being evaluated in order to over-

come these limitations. Technologies under development for the study of the colon include the Invendoscope™, the Video Capsule Endoscopy and the Aeroscope.

The Invendoscope™ (Invendo Medical, Kissing, Germany) is a single-use colonoscope based on motor driven inverted sleeve technology with a working channel^[17]. The results of a single-arm, pilot study on this device conducted on 39 healthy volunteers showed absence of pain in 92% of patients undergoing endoscopy; the cecum was reached in 82% of cases, after a mean time of 23 min^[17]. However, no data concerning its diagnostic accuracy are currently available^[17].

The Video Capsule Endoscopy (Given Imaging Ltd., Yoqneam, Israel) is a pill-size capsule, activated upon swallowing, which records images of the colonic mucosa^[18]. In a pilot study on 41 patients, this device showed a PPV of 59% and a NPV of 84% with respect to standard colonoscopy, with a specificity of 70%^[18]. These results were overall confirmed in a larger, recently published multicenter study; however, in this study the sensitivity of Visual Capsule Endoscopy was lower than that associated with standard colonoscopy^[15]. Moreover, this device cannot clear colonic debris during the procedure or insufflate air into collapsed intestines^[19].

Last, the Aeroscope (GI View Ltd, Ramat Gan, Israel) is a self-propelling, disposable endoscope, that uses low-pressure carbon dioxide to propel a balloon device through the colon, thus facilitating the motion of the colonoscope and reducing discomfort, pain and the risk of perforation^[20]. In a study conducted with 12 volunteers, this device reached the caecum in 83% of cases, after a mean time of 14 min. However, 17% of patients requested analgesia, and 33% experienced symptoms consistent with a vagal reaction, including sweating and bloating^[20].

The present study lends support to a possible introduction of the ES into clinical practice. In a previous pilot study, conducted in 40 patients, the ES was associated with significantly lower pain intensity and less discomfort, when compared to standard colonoscopy (pain intensity 0.9 vs 6.9; discomfort 1.1 vs 6.8; both parameters were evaluated on a 1-10 scale)^[14]. The high diagnostic accuracy and the lack of need for sedation reported in the present study during the ES procedure may represent further advantages of this technology. In particular, we believe that the reduced need for sedation may have a particular importance: it has been suggested that sedation may be associated with an increase in the onset of cardiopulmonary events and of unintended deep sedation^[4,6], although these findings were challenged by a recent meta-analysis^[21]. Noteworthy, the ES probe is a single-use device, thus limiting the risk of cross-infections and reducing the overall examination time, since no decontamination is required. Moreover, a single endoscopist may perform the entire procedure, without the need of any assistance by nurses.

However, it must be pointed out that the ES was associated with a lower rate of cecum reach, a more frequent incomplete view of the colon and a longer time to perform the examination than standard colonoscopy. In addition, the current version of this device does not allow

the endoscopist to perform polypectomy or biopsies.

We speculate that the higher number of patients with insufficient cleaning during the ES procedure than during the standard colonoscopy may be due to the smaller diameter of the suction device of the ES, when compared to that of the standard video-colonoscopy (1 mm vs 3.2 mm, respectively). Moreover, other potential limitations may be also related to low level of training with the ES, since the endoscopist performed > 500 colonoscopies and only > 20 ES in models and pigs with “similar human anatomy”.

This study has some limitations that must be acknowledged. First, it was performed in an overall limited number of patients; however, pilot studies with a similar or even smaller sample size have been conducted to evaluate other colonoscopy devices^[17,18,20]. Larger studies are required for a more complete evaluation of the ES. Second, inclusion and exclusion criteria were not stringent, potentially limiting the robustness of the analysis; however, this decision was taken in order to better reproduce clinical practice, even in an experimental setting. Third, the ES was compared only with a standard colonoscopic procedure, and not with any other new devices for colonoscopy. However, even if head-to-head comparisons with such devices is still lacking, and the available pieces of evidence do not permit us to retrieve definite findings, the results obtained with the ES may be preliminarily considered at least comparable with those observed with other alternative systems for colonoscopy^[17-20].

In conclusion, the ES has shown a high diagnostic accuracy, overall comparable to that reported with standard colonoscopy, and it appeared to be not associated with significant pain/discomfort^[14] or with the need for sedation. Although ES seems to show potential shortcomings such as lower cecum intubation rate and/or long duration of endoscopy, it may be considered a promising alternative to standard colonoscopy in the detection of colonic polyps, even if introduction of a tool to perform polypectomy or biopsies is advisable. On this basis, it may be considered a promising alternative to standard colonoscopy in the detection of colonic polyps.

It has been suggested that the introduction of this diagnostic instrument into clinical practice could facilitate the adoption of colonoscopy as first-level screening, with a possible reduction in the incidence of colon cancer-induced mortality^[14]. If larger studies, which should also evaluate the optimal bowel preparation conditions and further investigate the need for sedation, will confirm the preliminary evidence collected so far, the ES could play an important role in the detection of colorectal cancer diseases.

COMMENTS

Background

Video-colonoscopy is considered the gold-standard for the diagnosis of colonic diseases, including carcinomas and polyps. However, this diagnostic technique presents some limitations, such as invasiveness and patient discomfort, which limit the adherence to programs for the early detection of colon carcinoma. Furthermore, standard colonoscopy may be associated with various procedural risks.

Research frontiers

Newer diagnostic techniques are advocated to overcome limitations of video-colonoscopy while maintaining a good diagnostic accuracy. The endotics system (ES) is a new robotic device composed of a workstation and a disposable probe, which gave promising results in a pilot study for the detection of colonic polyps. The research hotspot is a head-to-head comparison of ES and standard colonoscopy in the diagnosis of polyps.

Innovations and breakthroughs

The present study lends support to a possible introduction of the ES into clinical practice. The high diagnostic accuracy and the lack of need for sedation reported in the present study during the ES procedure may represent further advantages of this technology.

Applications

The ES has shown a high diagnostic accuracy, overall comparable to that reported with standard colonoscopy, and it appeared to be not associated with significant pain/discomfort or with the need for sedation. It has been suggested that the introduction of this diagnostic instrument into clinical practice could facilitate the adoption of colonoscopy as a first-level screening procedure, with a possible reduction in the incidence of colon cancer-induced mortality.

Terminology

The ES: is a new medical device for diagnostic colonoscopy, composed of a workstation and a hand-held console which drives a steerable probe through the colon lumen. Standard preparation to colonoscopy: a fiber-free diet in the seven days preceding the examination and oral administration of phosphate sodium lavage solution (80 mL in 2000 mL of water until evacuation of clear yellowish fluid) on the day before the examination.

Peer review

The present study described a new device for diagnostic colonoscopy, named "ES". The authors aimed to compare ES with video-colonoscopy in regard to the detection rate of polyps. Moreover, use of sedation, cecum intubation rate and duration of endoscopy were assessed. The authors concluded that ES allowed the visualization of the entire colonic mucosa in most patients, with good sensitivity/specificity for the detection of lesions and without requiring sedation. The study is well-written and designed.

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