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Computed tomographic colonography in subjects with positive faecal occult blood test refusing optical colonoscopy

Lapo Sali[a,*], Grazia Grazzini[b], Leonardo Ventura[b], Massimo Falchini[a], Alessandra Borgheresi[a], Guido Castiglione[b], Michele Grimaldi[a], Nicola Ianniciello[c], Beatrice Mallardi[b], Marco Zappa[b], Mario Mascalchi[a]

[a] Radiodiagnostic Section, Department of Clinical Physiopathology, University of Florence, Viale G. Pieraccini 6, 50139 Florence, Italy
[b] Cancer Research and Prevention Institute (ISPO), Via Cosimo il Vecchio 2, 50139 Florence, Italy
[c] Nuovo San Giovanni di Dio Hospital, Via Torregalli 3, 50124 Florence, Italy

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ABSTRACT

Background: Refusal of colonoscopy is a drawback of colorectal cancer screening programmes based on faecal occult blood test. Computed-tomographic-colonography is generally more accepted than colonoscopy.
Aim: To compare adherence to computed-tomographic-colonography and second-invitation colonoscopy in subjects with positive faecal test refusing colonoscopy.
Methods: We performed a prospective study in 198 subjects with positive faecal test who refused first referral to colonoscopy in one endoscopy service of the Florence screening programme. Subjects were randomly invited to computed-tomographic-colonography ($n = 100$) or re-invited to colonoscopy ($n = 98$). Mail invitation was followed by a questionnaire administered by phone. Computed-tomographic-colonography findings were verified with colonoscopy.
Results: 32 subjects could not be reached, 71 (35.9%) had undergone colonoscopy on their own; 4 were excluded for contraindications; 30/48 (62.5%) in the computed-tomographic-colonography arm and 11/43 (25.6%) in the colonoscopy arm accepted the proposed examinations ($p < 0.001$). Four advanced adenomas and 1 cancer were found in the 28 subjects who ultimately underwent computed-tomographic-colonography and 2 advanced adenomas and 2 cancers in the 9 subjects who ultimately underwent second-invitation colonoscopy.
Conclusion: Subjects with positive faecal occult blood test refusing colonoscopy show a higher adherence to computed-tomographic-colonography than to second invitation colonoscopy.

1. Introduction

Colorectal cancer (CRC) is the second cause of cancer-related mortality in Europe [1]. Randomized clinical trials have demonstrated that screening with faecal occult blood test (FOBT) reduces mortality for CRC [2]. Accordingly, population-based screening with FOBT is currently recommended by the Council of European Union [3] and has been implemented in many countries, including Italy.

Subjects with a positive FOBT are referred to optical colonoscopy, which is the definitive examination for ascertainment of CRC since it allows exploration of the entire colon, removal of polyps and histological diagnosis. Adherence to colonoscopy in subjects with positive screening FOBT is incomplete, ranging between 72.9% and 92% [4,5]. Incomplete adherence represents a critical issue of FOBT-based screening programmes for CRC. In fact, taking into account that immunochemical FOBT has a positive predictive value (PPV) for advanced adenoma and CRC ranging from 32.5% to 51.8% [6,7], a non-negligible number of subjects at high risk of having significant rectal and colonic lesions potentially escapes timely diagnosis and treatment.

Computed-tomographic-colonography (CTC) is a pan-colonic examination that has a sensitivity of 88% in detecting large (≥10 mm) adenomas and 83% for 6–9 mm adenomas in asymptomatic subjects [8] and a high negative predictive value (range 84–93.3%) in subjects with positive FOBT [9–11]. In general CTC causes little discomfort [12,13] and was more accepted than colonoscopy by subjects participating in a recent randomized trial of CRC screening [14]. Moreover, CTC can be executed with limited bowel preparation [15]. For these reasons CTC, although not allowing a definitive diagnosis of CRC or adenoma, could theoretically represent a valuable tool to enhance attendance to a pan-colonic examination in subjects with positive FOBT who refuse colonoscopy.

* Corresponding author. Tel.: +39 0554271404; fax: +39 0554271413.
E-mail address: lapo.sali@unifi.it (L. Sali).

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We compared adherence to CTC versus re-invitation to colonoscopy in subjects with positive FOBT who refused first recommendation to undergo colonoscopy in a population-based screening programme of CRC.

2. Materials and methods

2.1. Study design and participants

This prospective study was conducted in the district of Florence, Italy, within the frame of the population-based programme for CRC screening of the Tuscany region, which is active since 2000 and is coordinated by Cancer Prevention and Research Institute (ISPO) [16]. The programme is addressed to all subjects aged 50–70 living in the Tuscany region who are invited via regular mail every second year to perform a one-day immunochemical FOBT. Subjects with negative FOBT are notified of their result by mail and re-invited to repeat screening after two years. Subjects with positive test receive a telephone consultation with a trained nurse who invites them to undergo colonoscopy in one of the 6 endoscopic units adhering to the CRC screening programme. In the Florence district screening programme 79% of FOBT-positive subjects are scheduled for colonoscopy within 2 months and 93% within 3 months [17]. Subjects refusing first invitation to colonoscopy receive a letter containing detailed report of their positive FOBT and an advice to undergo colonoscopy.

The study protocol was approved by our institutional review board and written informed consent was obtained from all participants. In a 22-month period (January 2010–October 2011) 145,000 subjects (at first or subsequent test round) were invited to the FOBT-based CRC screening programme in the district of Florence. Participation of invited population was 56% (81,200 subjects) [17]. All FOBT-positive subjects who were originally referred for colonoscopy to one of the 6 endoscopy services adhering to the CRC screening programme, located at ISPO, were considered eligible for the study. After at least two months since the date of refusal, these subjects were randomly assigned (1:1) to receive by mail an invitation to undergo CTC or a re-invitation to undergo colonoscopy.

The invitation letter contained information about the risk of CRC associated with a positive FOBT, specified the test to which the subjects were invited (CTC or colonoscopy) and announced a subsequent phone contact by a physician. In the latter a semi-structured questionnaire was administered to all subjects who consented to complete it, before acceptance of the proposed CTC or colonoscopy examination. The questionnaire investigated whether the subject had performed any examinations, in particular colonoscopy, in the interval time between first refusal and the phone interview and reasons for declining the first colonoscopy invitation at ISPO endoscopy service. After explanation of the characteristics of the CTC or colonoscopy, and the related intestinal preparations, the individuals who provided consent were scheduled to undergo CTC (Radiodiagnostic Section, Department of Clinical Physiopathology, University of Florence) or colonoscopy (Endoscopy Unit at ISPO).

The results of CTC were communicated to the subject by phone and by a subsequent mail letter. Subjects with positive CTC were invited to undergo colonoscopy for verification and possible histological evaluation of the CTC findings. The results of second-invitation colonoscopy were managed as usual in FOBT-positive subjects.

2.2. Data analysis

Results of CTC and colonoscopy (including the colonoscopy performed by the subject on his/her own in endoscopy services outside the screening programme) were reported on a per-subject basis. Lesions verified at colonoscopy were assumed as definitive results of CTC arm. Subjects were stratified according to the histology of the most advanced colonic lesion (cancer, advanced adenoma, non-advanced adenoma). Advanced adenoma was defined as any adenoma larger than 9 mm and/or with a villous component greater than 20%, and/or with severe dysplasia.

The analysis was performed using the Stata software version 12. The chi-squared test was used to evaluate the statistical significance of the differences between randomized groups.

2.3. CTC

CTC was performed using a reduced cathartic preparation, which consisted in the administration of 13.8 g of Macrogol 3350 (Movicol; Norgine, Milan, Italy) diluted in a glass of water three times a day for three days before examination. Subjects were also asked to follow a low residue diet for 3 days [18].

All subjects, except those with contraindications, received intravenously 30 mg of scopolamine butylbromid (Buscopan; Boehringer Ingelheim, Florence, Italy) before colonic insufflation. Colonic distension was obtained with manual insufflation of room air performed by a radiology resident.

Both supine and prone CT scans were obtained in all subjects. Colonic distension was evaluated with an anterior–posterior scout view in both supine and prone position, and additional air was inflated using a manual bulb if distension was unsatisfactory. Intravenous contrast medium was not used.

CTC was performed with a 64-MDCT scanner (Sensation 64; Siemens, Erlangen, Germany) using a low dose protocol (detector configuration of 32×0.6 mm, 120 kVp, 50 effective mAs, tube rotation time of 500 ms and a pitch of 1.4). Data were reconstructed using a slice thickness of 1 mm with a reconstruction increment of 1 mm. Estimated effective dose for the examination was 3.4 mSv (CTPatient Dosimetry Calculator, ImPACT; measures executed on Monte Carlo Phantom).

The images of each examination were transferred to a dedicated workstation (SYNGO; Siemens, Erlangen, Germany). The same reader, who had previously read about 200 CTCs, interpreted all images on the workstation using a primary 2-dimensional approach.

All lesions detected at CTC were localized according to their segmental location in the colon and measured taking into account their maximum diameter on two-dimensional images viewed with a bone window (level 400 HU, width 2000 HU). CTC results were classified according to the CTC Reporting and Data System (C-RADS) [19]. In case of inadequate examination (C-RADS 0), reasons for poor quality were annotated (faecal residues, liquid residues, colonic wall collapse). All subjects with colonic masses (C-RADS 4) or at least one polyp equal to or larger than 6 mm (C-RADS 2–3) were invited to undergo colonoscopy. Subjects with a negative CTC (C-RADS 1) were scheduled for standard follow-up (FOBT at 5 years). Major extra-colonic findings were reported (C-RADS E3-E4).

2.4. Optical colonoscopy

Bowel preparation was obtained with 2 L of a polyethyleneglycole solution (Moviprep; Norgine, Milan, Italy) administered the day before the procedure and a low residue diet for 5 days. An endoscopist with particular experience in CRC screening performed colonoscopy without or with deep sedation with Propofol (Diprivan; AstraZeneca, Milan, Italy), according to subject's preference. A standard commercial video colonoscope (EC-250 WI5; Fujinon, Wayne, NJ USA) was inserted to the caecum and sequentially withdrawn segment by segment for lesion recognition. Lesions detected were localized according to their segmental location and measured