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Correlation between adenoma detection rate in colonoscopy- and fecal immunochemical testing-based colorectal cancer screening programs

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Abstract

Background: The adenoma detection rate (ADR) is the main quality indicator of colonoscopy. The ADR recommended in fecal immunochemical testing (FIT)-based colorectal cancer screening programs is unknown.

Methods: Using the COLONPREV (NCT00906997) study dataset, we performed a post-hoc analysis to determine if there was a correlation between the ADR in primary and work-up colonoscopy, and the equivalent figure to the minimal 20% ADR recommended. Colonoscopy was performed in 5722 individuals: 5059 as primary strategy and 663 after a positive FIT result (OC-Sensor^{TM}; cut-off level 15 μg/g of feces). We developed a predictive model based on a multivariable lineal regression analysis including confounding variables.

Results: The median ADR was 31% (range, 14%–51%) in the colonoscopy group and 55% (range, 21%–83%) in the FIT group. There was a positive correlation in the ADR between primary and work-up colonoscopy (Pearson's coefficient 0.716; $p < 0.001$). ADR in the FIT group was independently related to ADR in the colonoscopy group: regression coefficient for colonoscopy ADR, 0.71 ($p = 0.009$); sex, 0.09 ($p = 0.09$); age, 0.3 ($p = 0.5$); and region 0.00 ($p = 0.9$). The equivalent figure to the 20% ADR was 45% (95% confidence interval, 35%–56%).

Conclusions: ADR in primary and work-up colonoscopy of a FIT-positive result are positively and significantly correlated.

Keywords

Colorectal adenoma, colorectal neoplasm, fecal immunochemical test, colonoscopy, colorectal cancer screening, adenoma detection rate

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Introduction

Colonoscopy plays a key role in colorectal cancer (CRC) screening, either as a primary strategy or work-up examination in other screening modalities (e.g. fecal immunochemical testing (FIT)-based screening programs). Indeed, colonoscopy can detect both premalignant and malignant lesions, and endoscopic polypectomy can effectively reduce CRC incidence and mortality.[1,2] However, colonoscopy is limited by low participation, bowel preparation, complications and variable detection rates.[3] The adenoma detection rate (ADR) has become the most important quality indicator of screening colonoscopy because it is directly related to key outcome measures, such as interval cancer incidence and mortality.[4,5] In addition, the ADR is a marker that indirectly reflects other surrogate quality indicators such as quality of preparation, completeness of colonoscopy, and withdrawal time.

Most CRC screening quality programs recommend that ADR should be, at least, 20% when colonoscopy is the primary screening strategy.[6] However, this figure cannot be used in the context of FIT-based CRC screening programs in which the number of adenomas detected in the FIT-based colonoscopy is clearly higher.[7] In this setting, although no study has specifically addressed this issue, it has been suggested to raise this figure to 40%.[6]

The COLONPREV study (NCT00906997) is a multicenter, randomized, controlled trial aimed at comparing the efficacy of one-time colonoscopy and biennial FIT for reducing CRC mortality.[8] Colonoscopies were performed by the same endoscopists in both arms in each hospital, following a specific, pre-established quality-assurance program.[8,9] The aim of the analysis we present is to determine whether there is a correlation between the ADR in primary and FIT-based screening colonoscopy and, if this correlation does exist, to establish the equivalent figure in FIT-based screening to the well-defined and accepted ADR of 20% in a colonoscopy-based setting.

Material and methods

This is a cross-sectional post-hoc analysis performed within the first round (June 2009–June 2011) of the COLONPREV study.[8] As was previously published, this study is being carried out in eight Spanish regions (Aragón, Basque Country, Canarias, Catalonia, Galicia, Madrid, Murcia and Valencia) with the participation of 15 tertiary hospitals. The study protocol was approved by the ethics committee of each hospital, and all participants provided written informed consent. Inclusion and exclusion criteria were described elsewhere.[8] In the FIT arm, participants collected one single sample that was analyzed with the automated semiquantitative OC-sensor^{TM} (Eiken Chemical, Tokyo, Japan), without specific diet or medication restrictions. Samples were processed as previously described[10] at each regional reference hospital. Individuals with $\geq$75 ng hemoglobin/ml of buffer solution ($\geq$15 μg/g of feces) were invited for colonoscopy.

In the first round, colonoscopy was performed in 5722 participants (in 5059 individuals as primary strategy and in 663 people as FIT-based examination after a FIT-positive result) by the same endoscopists in both arms in each hospital, and following a specific, pre-established quality-assurance program.[8,9] All colonoscopies were performed by experienced endoscopists (individual experience >200 colonoscopies per year). The mean withdrawal time in normal colonoscopies was 8.6 (±3.9) minutes, cecal intubation was achieved in 94.9% of the colonoscopies and colon cleansing was considered adequate in 97.9% of the colonoscopies.[9] Colonoscopies were performed using standard white light video equipment. Adenoma was diagnosed by pathological evaluation of retrieved polyps. The ADR was defined as the proportion of individuals with at least one detected adenoma among those tested.

In order to perform this analysis, we calculated the ADR in each age- (50–59 and 60–69 years old), sex- and region-based subgroup both in primary and FIT-based colonoscopy. Before performing a lineal regression analysis, we assessed whether the ADR had a normal distribution with the Kolmogorov-Smirnov test, and whether there were differences in the mean ADR and variance according to the number of colonoscopies (median) in primary and FIT-based colonoscopy arms with the Student t test and the F-test. Thereafter, we calculated the Pearson's correlation coefficient between both groups. Finally, we developed a predictive model based on a multivariable lineal regression analysis including the confounding variables (i.e. age, sex and region). On the basis of this predictive model, we determined the ADR in FIT-based colonoscopy of a FIT-based screening program equivalent to the most commonly accepted 20% ADR in primary colonoscopy, as well as to the figures recently recommended by the American Society for Gastrointestinal Endoscopy (ASGE) in the same setting (i.e. 25% overall, 30% in men, 20% in women).[11] Additionally, we determined if there were differences in the ADR in FIT-based colonoscopy according to the quartile distribution of the ADR in primary colonoscopy and inversely using the Kruskal-Wallis test. Differences were considered statistically significant if the p value was less than 0.05. All analyses were performed using the SPSS statistical software, version 15.0 (SPSS Inc, Chicago, IL, USA).

Table 1. Distribution of the adenoma detection rate (ADR) and the number of colonoscopies in each region subgroup according to age and sex and in both work-up and primary colonoscopy groups.

		Work-up colonoscopy		Primary colonoscopy	
		ADR (%)	Number	ADR (%)	Number
Age (years)	50–59	53 (21–78)	16 (9–35)	28 (14–47)	158.5 (120–288)
	60–69	56 (38–83)	22.5 (9–50)	36 (16–51)	138 (88–246)
Sex	Male	67 (26–78)	17.5 (9–50)	37 (22–51)	156 (89–261)
	Female	45 (21–83)	18 (9–29)	23 (14–51)	155.5 (88–288)
Overall		55 (21–83)	17.5 (9–50)	55 (21–83)	155.5 (88–288)

Data are expressed as the median and range.

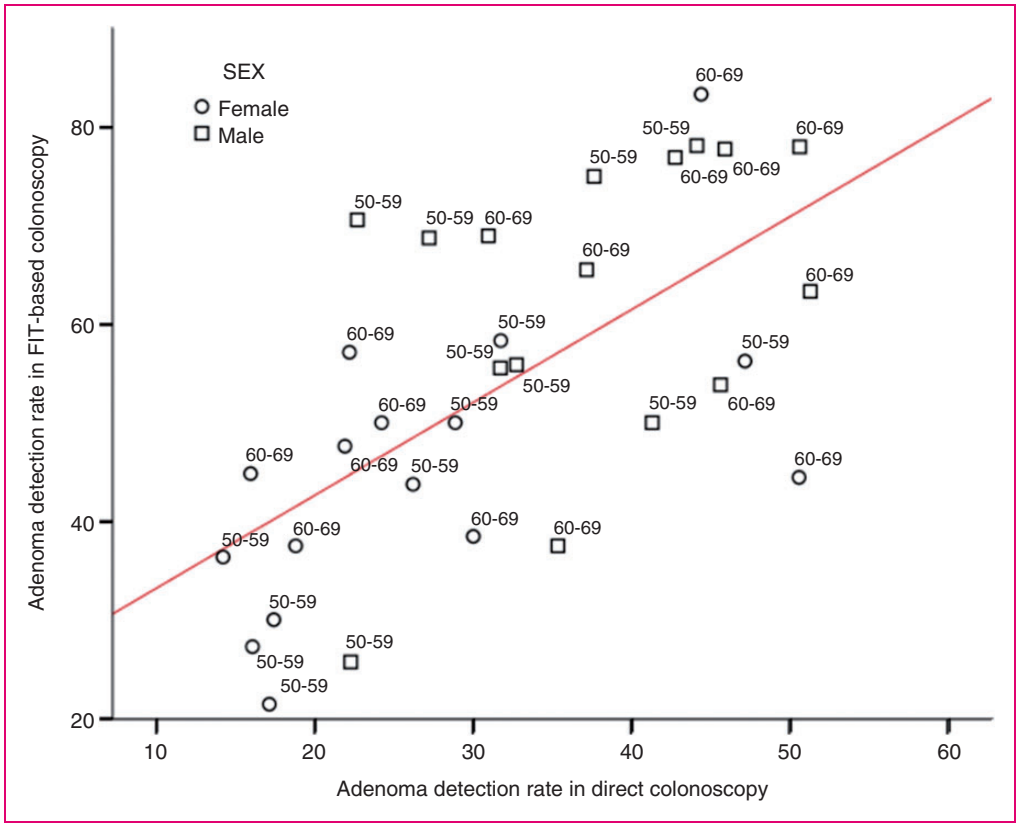

Figure 1. Distribution of the adenoma detection rate by age group (50–59 and 60–69 years old), sex (women in blue circles and men in green ones) and Spanish region both in primary and fecal immunochemical test (FIT)-based colonoscopy. The regression line is shown.

Results

The median number of colonoscopies by age and sex are shown in Table 1. The ADR had a normal distribution in primary and FIT-based colonoscopy groups ($p = 0.9$), and there were neither statistical significant differences in the variance ($p = 0.7$) nor in the mean ADR in each group ($p = 0.4$ and $p = 0.7$, respectively), according to the number of colonoscopies included in the FIT-based colonoscopy group. There was a positive correlation in the ADR between primary and FIT-based colonoscopy (Pearson's coefficient, 0.716; 95% confidence interval (95% CI), 0.378–0.819; $p < 0.001$). In Figure 1, we show the distribution of the ADR in all evaluated subgroups, as well as the corresponding regression line.

The coefficient of multiple correlation of the predictive multivariable lineal regression model was 0.68. In this model, the ADR in FIT-based colonoscopy was independently related to the corresponding figure in primary colonoscopy (regression coefficient, 0.71, 95% CI, 0.19–1.22; $p = 0.009$). The regression

coefficients of potential confounders were: sex (male), 0.09 (95% CI, −0.1 to 0.21; $p = 0.09$); age (60–69 years old), 0.3 (95% CI, −0.07 to 0.13; $p = 0.5$); and region, 0.00 (95% CI, −0.01 to 0.01; $p = 0.9$). No collinearity was found among the variables included in the regression model. On the basis of the above-mentioned multivariable regression analysis, estimated ADR in FIT-based colonoscopy equivalent to the 20% ADR in primary colonoscopy was 45% (95% CI, 35%–57%). In addition, estimated ADR in FIT-based colonoscopy equivalent to the figures recommended by the ASGE in primary colonoscopy were 49% (95% CI, 36%–62%) overall, 54% (95% CI, 39%–69%) in men, and 44% (95% CI, 34%–54%) in women.

According to the quartile distribution of the ADR in direct colonoscopy, the ADR in the FIT group ranged from $37.7 \pm 11.7\%$ in the lowest quartile to $66.9 \pm 14.3\%$ in the highest quartile ($p = 0.06$). Inversely, the ADR in the primary colonoscopy ranged from $21.3 \pm 7.4\%$ in the lowest FIT group quartile to $39.8 \pm 9.1\%$ in the highest quartile ($p = 0.01$).

Discussion

In this cross-sectional post-hoc analysis, we demonstrated that there is a positive and significant correlation between the ADR in primary and FIT-based colonoscopies. According to this correlation, we determined that a 45% ADR in FIT-based CRC screening programs seems equivalent, in terms of quality indicator, to the well-accepted 20% figure in colonoscopy screening. In fact, these findings are concordant with the mean ADR found in other CRC screening programs based on fecal occult blood testing: 44.8% in the Italian screening program (i.e. FIT based) and 46.5% in the National Health System Bowel Cancer Screening Programme in the United Kingdom (UK) (i.e. guaiac based).[12,13]

Our analysis has two main strengths. First, data were obtained from the two arms of a randomized controlled trial comparing the most widely accepted options for average-risk CRC screening in a population-based scenario,[8] thus representing a unique opportunity to match the ADR of both strategies. Second, colonoscopies were performed by the same endoscopists in both arms and followed a strict quality-assurance program,[8,9] thus guaranteeing the comparability of results. We are not aware of any other study of similar characteristics from which this comparison could be established.

By contrast, we are aware of some limitations. First, the ADR was calculated by age group, sex and geographic region, but not by each specific endoscopist because of the relatively small number of colonoscopies in the FIT group performed individually. However, this potential weakness was somehow overcome taking into account the large sample size of the COLONPREV study, the statistical analysis employed and, more important, the fact that all colonoscopies were performed by the same group of endoscopists in each center. Second, although there was a strong and independent correlation between the ADR in FIT-based colonoscopy and the corresponding figure in primary colonoscopy, we cannot infer that the selected value for FIT-based screening would also correlate with those outcomes associated with this parameter (i.e. interval cancer and mortality) in the latter setting.[4,5] However, while prospective studies are needed to evaluate this aspect and, therefore, to validate the selected value, our data represent a reliable starting point to be used in current CRC screening programs. Finally, it is important to keep in mind that these results were obtained in the first round of a FIT-based screening program using a one-sample strategy with a 15 µg of hemoglobin/g of feces cut-off and, therefore, our correlation should be limited to this scenario. In fact, the positive predictive value of the FIT strategy is modified according to the threshold used and the number of samples analyzed.[14–16] In that sense, although the two specific conditions employed in our study are among the most common in FIT-based screening programs, it would be feasible to calculate the specific ADR for other conditions using the corresponding positive predictive value for adenoma as conversion factor. The same approach could be used to correct the fact that our data were derived from the first screening round, in which the prevalence of neoplastic lesions is higher,[12] thus universalizing the corresponding figures.

In conclusion, the positive and significant correlation between the ADR in primary and FIT-based colonoscopy provides the rationale for setting this quality indicator at 45% in the first round of FIT-based (i.e. 15 µg of hemoglobin/g of feces cut-off) CRC screening programs.

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J.C. and A.C. designed the analysis, performed the statistical analysis and wrote the article. M.A, L.B, F.C, R.J, A.L, JD.M, D.S and E.Q. participated in the acquisition of data, interpretation of data, performed critical revision of the manuscript, and obtained funding, technical or material support. All authors approved the final version of the article and decided to send it for publication. Finally, all authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Conflict of interest

None declared.

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Appendix

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